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INTRAVENOUS INJECTION OF POOLED NORMAL PLASMA OR SERUM

IS IT DANGEROUS?

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An extensive, worldwide experience has demonstrated that the therapeutic intravenous administration of large amounts of properly prepared, pooled human plasma or serum to patients belonging to all four blood groups is followed by only a small percentage of reactions of any kind. Most of these reactions are either so mild as to be insignificant or only moderate in degree, insufficient to cause any real harm to the patient. Certainly it has been shown that no one in genuine need of this type of intravenous therapy should be denied it because of the possible occurrence of one of these reactions.

Nevertheless, several recent publications [1] have questioned the opinion derived from this experience, on the basis of the possible danger from the injection of incompatible agglutinins or incompatible A or B substances.

The important question and, in fact, the only question is whether it is safe to administer pooled plasma or serum intravenously in large amounts to an individual who is in urgent need of this type of therapy regardless of his blood group. The corollary of this is: Are possible incompatible agglutinins or the agglutinogens in A or B substances present in pooled serum or plasma in sufficiently strong concentration to be a possible danger to the patient?

Plasma or serum prepared on a large scale can be produced satisfactorily and economically only when large pools are prepared by mixing the material obtained from many donors belonging to all four blood groups.

Only in small blood banks does occasion ever arise to use plasma obtained from only one donor. Whereas the problem of the advisability of administering plasma obtained from a single donor, regardless of the blood group of the recipient, is an important one for a hospital this does not particularly concern us here.

We must discuss mainly the possible danger from the intravenous injection of large amounts of pooled plasma or serum containing low titers of incompatible agglutinins that might cause specific intravascular phenomena and therefore possibly injure the patient, and whether either the A or B substances can be present in sufficiently large amounts to cause a serious reaction or harm to a patient receiving these intravenously.

It may be well to make clear at the outset that it is quite well recognized that any material injected intravenously may cause a fever-chill, or even more severe, reaction. In fact, the larger a physician's experience the more he realizes that if he gives enough intravenous injections, even of the most carefully prepared isotonic saline and dextrose solutions, to enough different patients, sooner or later he will encounter a fever-chill reaction. The better the technic of preparing and administering all intravenous therapeutic agents, and making certain that the solutions are free of the usual pyrogenic substances, the less often will these reactions occur. In many hospitals, hundreds of injections of intravenous solutions have been carried out without a single reaction, and then one or several reactions have occurred.

It is well known that one cannot prevent the occurrence of nonhemolytic reactions after the administration of even the most carefully checked and proved, compatible blood transfusions. The general experience is that these reactions cannot be reduced to a level lower than about 3 per cent. This refers only to fever-chill reactions, or even more severe ones with urticaria, severe back or chest pains, and the like. If even milder reactions are counted, the total minimal percentage is between 6 and 7. However, even with full recognition of this, properly carried out blood transfusions are a well accepted, widely used therapeutic agent and are not infrequently life saving. These possibilities of reactions have merely caused every one to take infinite care in compatibility tests, in blood typing, and in careful technic and have not deterred physicians from giving transfusions when these are indicated.

The reactions referred to can be called nonspecific reactions. By this term it is meant that the reactions are not caused by specific agglutinogens or antibodies, such as A and B substances or by isohemolysins, isoagglutinins, anti Rh substances and so on. If a reaction is attributed to these agglutinogens or antibodies, data must be presented proving this. Aubert [2] has reached the same conclusion.

For example, if a reaction is considered caused by an incompatible transfusion of blood, this incompatibility must be demonstrated. If a reaction is termed a hemo-

From the Human Serum Division of the Public Research Institute of the City of New York, Inc.

1. Polayes, S. H., and Squillace, J. A.: Near Fatal Reaction to Transfusion with Dried Human Plasma Solution, J. A. M. A. **118:** 1050 (March 28) 1942. Toxicity of Human Plasma, editorial, ibid. **120:** 206 (Sept. 19) 1942. Levine, Milton, and State, David: A and B Substances as a Cause of Reactions Following Human Plasma Transfusions, ibid. **120:** 275 (Sept.) 1942.

2. Aubert, E. F.; Boorman, K. E., and Dodd, B. E.: The Agglutinin Inhibiting Substance in Human Serum, J. Path. & Bact. **54:** 89-104 (Jan.) 1942. Aubert, E. F.; Boorman, K. E.; Dodd, B. E., and Loutit, J. F.: The Universal Donor with High Titer Isoagglutinins: The Effect of Anti A Isoagglutinins on Recipients of Group A, Brit. M. J. **1:** 659 (May 30) 1942.

lytic reaction, actual hemolysis must be demonstrated in the form either of hemoglobinemia or of hemoglobinuria. If the reaction is believed to be caused by the injection of incompatible agglutinins, then phenomena resulting from the incompatible agglutinins must be demonstrated in the patient or in the patient's blood, and not merely by in vitro tests with the patient's blood and a portion of the injected serum or plasma. If simple intravenous solutions are used, such as isotonic solution of sodium chloride, and a reaction occurs it is usually caused by pyrogenic substances in the solution or in the intravenous apparatus, and the same may be the cause of reactions following proved compatible blood transfusions or injections of plasma or serum.

There are two points which need discussion first: 1. What is the level of the titers of anti A and anti B agglutinins in routine pools of serum or plasma? 2. Is there any danger from incompatible isoagglutinins to a patient receiving intravenouly a large amount of either this pooled material or high titered single specimens of serum or plasma?

The agglutinin titer of eleven mixed pools of serum was determined (table 1), no care being taken to adjust the relative number of samples from the different blood groups in each pool.[3] The agglutinin titer was determined by Davidsohn's method,[4] which is a test tube technic, the end point being determined by observation under the low power microscope of the test tube placed on its side on the stage of the microscope. The result is recorded as the highest dilution in which clumps of three or more cells are seen, provided no clumping at all is observed in the next highest dilution. We have found this technic very accurate, and in duplicate tests it did not vary more than one dilution above or below the final reading. We believe it gives a reading of an even higher titer than the usual slide test read with the microscope.

TABLE 1.—*The Agglutinin Titer of Routine Pools of Normal Serums from All Four Blood Groups*

Pool	No. of Serums in Pool	Percentage Belonging to Each Blood Type				Agglutinin Titer of Pool	
		O	A	B	AB	Anti A	Anti B
S- 2	72	45.9	38.9	11.1	4.1	1:14	1:14
S- 3	49	38.7	57.1	2.1	2.1	1:14	1:14
S- 4	48	29.2	58.3	10.4	2.1	1:3	1:6
S- 5	45	40.0	42.2	13.4	4.4	1:7	1:7
S- 6	44	36.3	50.0	11.4	2.3	1:4	1:7
S- 7	49	63.3	32.7	2.0	2.0	1:14	1:28
S- 8	48	41.7	43.8	14.5	...	1:4	1:14
S- 9	44	45.4	34.0	18.4	2.2	1:7	1:6
S-10	49	47.0	49.0	4.0	...	1:7	1:14
S-11	11	45.5	36.3	9.1	9.1	1:7	1:14
S-12	48	56.2	29.2	14.6	...	1:28	1:14
S-13	41	48.8	31.7	7.3	12.2	1:14	1:14
S-16	10	40.0	30.0	30.0	....	1:28	1:7
Average		44.5	41.0	11.4	3.1	1:11.7	1:12.2

The number of individual serums in each pool varied from ten to forty-nine. In all of the pools the agglutinin titer was low, the anti A agglutinin varying from 1:3 to 1:28, the anti B from 1:6 to 1:28. Since B and O serums in general are likely to have a higher titer of anti A agglutinins than the anti B agglutinins in A and O serums, it is interesting and important that the final levels of these two agglutinins in the mixed pools are approximately the same.

It has been demonstrated[5] that there is definite neutralization or "suppression" of hemolysins and agglutinins when serums or plasmas of different blood groups are mixed together. This undoubtedly is caused through the neutralization of the antibodies by the dissolved A or B substances present in solution.

Dr. D. G. Gemeroy has investigated this same problem, but even more extensively, and though his studies are in process of publication he has given permission to mention his results. His work was carried out at the Connaught Laboratories in collaboration with Prof. C. H. Best on pooled serums prepared by the Canadian Human Serum Project. Originally the blood types of serums added to each pool were in the same percentages as those in which these blood types occurred in the general population of Toronto. Each pool consisted of fifty serums with the following percentages of blood types in each pool: O 46 per cent, A 41 per cent, B 10 per cent, AB 3 per cent. The anti A agglutinin titers varied from 1:10 to 1:30, the anti B from 1:10 to 1:60. The technic was similar to the one we used.[6]

Since it was time consuming to select these serums in these proportions and much easier to pool the serums consecutively, the agglutinin titers were then determined first on several pools and later on many more, where fifty serums obtained consecutively were mixed regardless of blood types, although these blood types had been determined. It was found that, although there was some variation in the percentages of the blood types in the different pools, the agglutinin titers nevertheless remained at practically the same level as those in the pools originally studied.

These results seem to us extremely important, as they demonstrate that if pools are prepared of a sufficient number of serums or plasmas selected indiscriminately one can be certain that the agglutinin titers of these will be extremely low. Whether one should be required routinely to determine agglutinin titers in these final pools is a question that will be discussed later.

We next come to a discussion as to whether there is any evidence that the intravenous injection of plasma or serum low in agglutinin content can cause intravascular phenomena which are injurious to the patient, and whether injury to the patient can result if even large amounts of high titered plasma or serum are used.

We[3] have investigated this problem to some extent, and Aubert and his co-workers have studied it even further.

Our study was carried out in three ways: 1. We repeated the work already referred to to determine the degree of suppression of agglutinins when pools are made of a number of samples of serum obtained from individuals belonging to the different blood groups. 2. We studied to what degree serum containing incompatible agglutinins could be diluted in whole citrated blood until the agglutinins are sufficiently diluted so that agglutination of cells does not occur. These mixtures were then stored in the ice box overnight and the supernatant serum was examined to find out whether

3. Thalhimer, William, and Myron, S.: Absorption of Isoagglutinins from Human Serum, Report to the American Human Serum Association, annual meeting, June 1940; The Fate of Incompatible Isoagglutinins Which Are Injected Intravenously, ibid.

4. Davidsohn, I.: Test for Infectious Mononucleosis, Am. J. Clin. Path., Tech. Supp. **2**: 56-60 (April) 1938.

5. Moss, W. L.: Studies on Isoagglutinins and Isohemolysins, Bull. Johns Hopkins Hosp. **21**: 63 (March) 1910. Levinson, S. O., and Cronheim, Anny: Suppression of Isoagglutinins and the Significance of This Phenomenon in Serum Transfusions, J. A. M. A. **114**: 2097 (May 25) 1940.

6. The serums were diluted in a similar manner in a series of marked test tubes. One drop of freshly prepared 1 per cent A or B suspensions was then added to each square of the serum dilutions on a large cell slide. The slides were then placed on a mechanical shaker and agitated for thirty minutes. The plates were then removed, the cells allowed to settle for ten minutes, and agglutinin titers determined microscopically. The test was set up in duplicate in parallel rows on the plate.

or not the agglutinins had been completely absorbed.

3. We injected intravenously therapeutic serums containing agglutinins incompatible with a patient's blood cells and followed the fate of the injected incompatible agglutinins in small samples of the patient's blood obtained immediately after administration of the serum and at subsequent intervals.

1. Our work was in agreement with the previous work that there is definite suppression of agglutinins when serum from the four blood groups are pooled. In none of these pools, as already mentioned, did we find an agglutinin titer higher than 1:28.

2. In table 2 there is found a protocol of a typical experiment in which agglutination was observed in vitro in a series of test tubes in which an incompatible serum was added to larger and larger amounts of citrated blood. In this experiment two serums were diluted with citrated A blood, one serum having an anti-A titer of 1:14 and the other 1:896.

It can be seen that even in a 1:1 mixture of the low titer serum and the blood there was no agglutination of the cells. In mixtures with the serum whose titer was 896, agglutination of cells was detectible in dilution as high as 1:80; that is, 1 part of serum with 79 parts of blood. However, agglutinins were completely removed in all dilutions from the supernatant plasma, which was examined the following day.

This experiment was repeated with three times concentrated serum prepared by making a pool consisting entirely of serum belonging to group O. The anti A titer of this concentrated serum was 1:224, and the anti B 1:112. In the mixtures of this serum with type A blood agglutination occurred in dilutions as high as 1:80, and with type B blood to dilutions as high as 1:20. The supernatant serum from these tests examined the next day showed not quite complete absorption of the agglutinins, since these were demonstrated in full strength serum against A cells from the mixture diluted 1:60 and against B cells from the mixture diluted 1:10.

One can see from the protocol given in table 2 that there was more complete absorption of agglutinins with a titer of 1:896 than with the three times concentrated serum whose agglutinin titer was considerably lower.

The foregoing findings will be referred to again in the discussion.

3. In 1938 Moureau, Balgairies and Christiaens[7] published apparently the first study of the fate of incompatible agglutinins injected intravenously. They transfused blood from universal donors with an unusually high anti A titer ranging up to 1:1,024 into recipients belonging to types A or AB. Samples of blood were obtained from the recipients immediately after the transfusion and at later intervals and were examined for the presence of agglutinated clumps of cells. Moureau and his co-workers were unable to find agglutinated cells in any of these samples. We were not familiar with their work when we commenced ours.

We took advantage of the opportunity to carry out this study on patients who were given intravenous therapeutic or prophylactic injections of pooled convalescent scarlet fever or measles serums (human).[8]

The observations were made only on patients belonging to types A, B or AB. The serums were injected into a vein in one arm, and samples were obtained with a fresh sterile syringe from a vein in the other arm immediately after the injection was completed and, in some instances, several hours later. Eight children and 7 adults received these serums. The amount injected varied from 50 to 100 cc. The titer of the incompatible agglutinins in the serums was as high as 1:896 in 1 instance, 1:448 in several other instances and considerably lower in others. The dilution of the serum injected in the total blood volume of the patient was calculated on the basis that the blood volume is one-tenth the weight of the individual. One child belonging to type A, weighing 40 pounds (18 Kg.), received 60 cc. of convalescent scarlet fever serum with an anti A agglutinin titer of 1:448. The calculated dilution of this amount of serum in the total blood of the recipient was 1:33 and in the plasma about 1:17. One adult belonging to type AB received 80 cc. of convalescent scarlet fever serum with an anti A agglutinin titer of 1:448 and anti B of 1:56. This volume of serum was diluted 1:74 in the patient's blood. Several children received a quantity of serum which was a thirtieth or a fortieth of their blood volume, and in some of the adults the dilution of the serum was larger.

Nevertheless, in none of these patients did reactions occur, and none of the samples of blood obtained immediately after the serum was injected showed agglutination of red cells or hemoglobinemia, nor was

TABLE 2.—*Agglutination Phenomena and Fate of Agglutinins When Incompatible High and Low Titered Agglutinating Serums Are Mixed with Citrated Blood*

Procedure: Serums 493A and 494A (type B) used in combination with type A blood and serum in the following tests.

Agglutination Titer of Serums Used

Serums Used	Cells	1:7	1:14	1:28	1:56	1:112	1:224	1:448	1:896	1:1,792	1:3,584	Control
493A (B)	A	+	+	—	—	—	—	—	—	—	—	—
494A (B)	A	+	+	+	+	+	+	+	+	—	—	—

Mixture of Citrated Blood and Incompatible Serums Observed for Agglutination of Cells

Dilution	1:2	1:5	1:10	1:20	1:40	1:80	1:160	1:320	Control Saline	
493A—B serum	1	1	1	1	1	1	1	1	1	These mixtures made,
A blood	1	4	9	19	39	79	159	319	1	allowed to stand two
Cell examination	—	—	—	—	—	—	—	—	—	hours, and then centri-
494A—B serum	1	1	1	1	1	1	1	1	1	fuged. Plasma remov-
A blood	1	4	9	19	39	79	159	319	1	ed and cells examined
Cell examination	+	+	+	+	+	+	—	—		for agglutination

The Supernatant Plasmas from Foregoing Experiment Tested for Incompatible Agglutinins

Serums Used	Cells	5:2	1:2	1:3	1:4	1:5	1:6	1:7	1:14	1:28	1:56	Control
493A (B) + A blood												
1:2	A	—	—	—	—	—	—	—	—	—	—	—
1:5	A	—	—	—	—	—	—	—	—	—	—	—
1:10	A	—	—	—	—	—	—	—	—	—	—	—
1:20	A	—	—	—	—	—	—	—	—	—	—	—
1:40	A	—	—	—	—	—	—	—	—	—	—	—
1:80	A	—	—	—	—	—	—	—	—	—	—	—
1:160	A	—	—	—	—	—	—	—	—	—	—	—
1:320	A	—	—	—	—	—	—	—	—	—	—	—
494A (B) + A blood												
1:2	A	—	—	—	—	—	—	—	—	—	—	—
1:5	A	—	—	—	—	—	—	—	—	—	—	—
1:10	A	—	—	—	—	—	—	—	—	—	—	—
1:20	A	—	—	—	—	—	—	—	—	—	—	—
1:40	A	—	—	—	—	—	—	—	—	—	—	—
1:80	A	—	—	—	—	—	—	—	—	—	—	—
1:160	A	—	—	—	—	—	—	—	—	—	—	—
1:320	A	—	—	—	—	—	—	—	—	—	—	—

7. Moureau, P.; Balgairies, E., and Christiaens, L.: Existe-t-il des donneurs universels dangereux? Presse méd. **46**: 958 (June 18) 1938.

8. Dr. I. F. Klein of the Willard Parker Hospital cooperated in this study.

it possible to demonstrate the presence of incompatible agglutinins in the serum obtained from these samples. These serums were all pooled serums even though the agglutinin titers of several were somewhat higher than the pooled serums already reported.

These negative laboratory findings correspond with the infrequency of reactions observed in an extensive experience obtained by many in New York, Chicago and other cities when scarlet fever convalescent serum (human) has been injected intravenously in the treatment of patients with scarlet fever. Some very sick children 4 to 6 years old have received 40 cc., and others 10 to 12 years old as much as 80 cc. in one injection. Several children 14 to 15 years old have received single injections of 100 cc. a day on eight to ten consecutive days. Only an occasional fever-chill reaction has been observed.

Whereas some of these reactions were unpleasant and disconcerting, none of them were followed by any harmful effect. They were all recovered from promptly, and most of the children went on to secure a beneficial therapeutic effect from the serum.

Aubert and his co-workers [2] have published two important investigations in this field. In their second study (the first investigation will be referred to later) they undertook to investigate whether there is a danger in transfusion of universal donor blood with a very high agglutinin titer into an individual belonging to type A, B or AB, for whom this agglutinin is incompatible. Instead of using high titered universal blood, since the cellular elements complicate the study, they injected high titered incompatible serum, and apparently the serum that they used was that which they developed in their previous work. The titers of several of the serums used were 1:32, 128 and 512; others ranged from 1:1,024 through 1:16,384. Only several subjects received the low titered serums, most of the 16 receiving the high titered ones. Samples of blood were taken immediately after injection from a vein in the opposite arm, and these were studied under a microscope for agglutination of cells, called "agglutinates" by the investigators. Careful observations were made of clinical reactions including, of course, fever and chills, presence of hemoglobinemia or hemoglobinuria, serum bilirubin and the fall of the red cell count of the recipient.

None of the recipients receiving as much as 450 cc. of serum of the titer less than 512 showed any agglutinates in the postinjection sample of blood. However, most of them who received from 20 to 500 cc. of serum with titers of 1:512 or higher did show agglutinates in the postinjection sample, and in 2 of them in samples taken after three and a half hours. The serum bilirubin rose in many, and the red cell count fell quite definitely in many. Hemoglobinemia and hemoglobinuria occurred in several. Chills occurred three times, headaches and fever above 100 F. nine times. "Five developed a syndrome, the most striking symptoms of which were moderate or severe aching pains across the small of the back, often radiating to the thighs, constricting sensations in the neck and chest, intestinal colic, and nausea."

They noted that several recipients of low titered and even agglutinin free serum had similar reactions, additional evidence that such reactions are not dependent on high titered incompatible agglutinins.

Figures from two of their tests are worth recording. A man belonging to type A, weighing 140 pounds (63.5 Kg.) received in twenty minutes 450 cc. of serum with an anti A titer of 128. This was about one-seventeenth his total blood volume. Nevertheless he had no reaction, and no agglutinates were found in his blood. A woman belonging to type A, weighing 120 pounds (54 Kg.), received in twenty-five minutes 500 cc. of serum with an anti A titer of 2,048. This was about one-twelfth her total blood volume. The highest her temperature reached was 99.5 F. and there were no subjective symptoms, but there were intravascular agglutinates present in large numbers, persisting for two hours. It is extremely interesting, as these investigators also note, that no detectable embolic phenomena whatever were caused by these agglutinates, some consisting of eight to ten red blood cells.

The only published study I have found of the intravenous injection of serum containing A or B substances besides that of Levine and State was the other study mentioned, carried out by Aubert and his co-workers. They injected intravenously from 100 to 350 cc. of A or B serum secured from a single individual into ten normal type O recipients. The object of this study was to determine whether the intravenous administration of A or B substance would stimulate the recipient to produce a definite increase in the corresponding anti-agglutinin. In all the recipients a definite specific and sometimes nonspecific increase in agglutinins occurred, in several instances to a titer of 1:8,000 or 1:16,000. Although these recipients were very carefully followed there is no mention that any suffered from any reactions at all. Certainly no mention was made of any reactions that might be attributed to the injection of incompatible A or B agglutinogens.

One of their interesting observations is what they term the "inhibition index" of a serum. By this they mean the ability of a serum to reduce the titer of incompatible agglutinins in another serum.

They clearly indicate that the inhibiting substance is dissolved A or B agglutinogen. They describe the inhibition index as follows: "The index of a serum is 8 if it reduced the titer of an agglutinin from 1:128 to 1:16 and 2 if it reduced the titer from 1:64 to 1:32. The index, therefore, represents the number of times the titer has been reduced." They do not consider this an absolute figure but as an approximate guide of the amount of incompatible substance present.

This should prove a useful method for determining at least approximately whether A or B substances are present in any appreciable amount in pooled serum or plasma. This study should be made and is of importance, since the question has been raised as to whether incompatible A or B substance can cause specific, deleterious reactions when present in plasma or serum that is administered intravenously.

It is sufficiently important to quote in full the summary arrived at by these investigators:

> The transfusion of conscious recipients of group A (12 cases) with considerable volumes of group O serum or plasma containing extremely potent anti A isoagglutinins did not produce any reaction which could be classed as dangerous. No evidence, therefore, was obtained that "incompatible" isoagglutinins are responsible for severe or fatal hemolytic reactions.
>
> In all these transfusions, however, there was some evidence of red cell destruction in the recipient, with the production of symptoms in some cases.
>
> Group O blood with an agglutinin titer of 512 and over is not recommended for recipients of other groups in non-emergency transfusions designed to raise the red cell count.

The agglutinogen present in the plasma of group A recipients is not an absolute protection against anti A agglutinins.

The isoagglutinin content of serum and plasma pools prepared by the technics used at the London Blood Supply Depots *can safely be ignored* [italics supplied].

COMMENT

It should be pointed out that several investigations have now demonstrated that when plasma or serum obtained from a sufficient number of individuals belonging to all four blood groups is pooled there is definite suppression of anti A and anti B agglutinins. The resultant titer of these might be anywhere from 1:6 to 1:60 but not any higher than this.

Type B serum with an anti A agglutinin titer of 1:896 showed agglutination in the test tube when this was mixed with citrated type A blood in a dilution of 79 parts of blood to 1 part of serum but not in higher dilutions. This demonstrated that in vitro even in a dilution of 1:80 agglutination of cells will occur. Nevertheless, Aubert and his co-workers found that, when a serum containing incompatible agglutinins to a titer of 1:2,048 was injected intravenously into a patient in the proportion of 1 part of serum to 12 parts of the entire blood volume, no reaction occurred and no intravascular agglutinates were formed.

Also in other studies described in the foregoing, when the fate of reasonably high titered agglutinins that had been injected intravenously was followed we found that the agglutinins disappeared almost immediately.

We believe that the evidence indicates that there are at least three mechanisms for neutralizing incompatible agglutinins that might be injected intravenously: 1. The agglutinins are suppressed to some extent by free agglutinogen in solution in the plasma. 2. Neutralization occurs by circulating cells; included in this must be the factor of the dilution of the injected agglutinins. 3. Since agglutinins are neutralized more readily when injected into a person's circulating blood than when added to blood in the test tube, there must be other agents to neutralize the incompatible agglutinins, such as the agglutinogens in fixed tissue cells. Just because plasma or serum will cause agglutination in the test tube is no proof that it also will cause agglutination when injected intravenously into a patient from whom the blood was obtained to carry out the test.

The evidence seems quite clear that therapeutic doses of pooled serum or plasma can be safely administered intravenously when indicated, regardless of the blood type of the recipient, provided the titer of the incompatible agglutinins is less than 1:512, and many times when the titer is even higher.

Evidence has been presented that both the anti A and anti B agglutinin titers of pooled plasma and serum are well below 512, probably in the neighborhood of 1:20 or 1:30 but never higher than 1:60.

In the case report of Polayes and Squillace the agglutinin titer of the pooled plasma injected intravenously was only 1:16 and, from the evidence presented here, could not possibly account for the reaction in the patient. There is no evidence in their report that this reaction was a hemolytic one. On the contrary, though a severe reaction, it had merely the characteristics of a nonspecific reaction, which at times is caused by the administration of simple intravenous solutions, compatible blood transfusions and the like.

The evidence presented by Levine and State that reactions are caused by the injection of A or B agglutinogen is far from conclusive. The type of reactions which they describe are general types of reactions and have no elements that could be characterized as specific. Furthermore, they have not demonstrated that a specific reaction occurred in the patient's blood stream. The skin test reaction which they describe can be produced by many substances, and there are many substances present in blood plasma besides A and B agglutinogens which might conceivably cause skin reactions.

They have omitted one very important control. They have not injected A or B substances or plasma containing A or B substances into patients belonging to type AB who do not have anti A or anti B agglutinins in their blood. If the injection of incompatible A or B substances is as dangerous as they believe it to be, one would expect that Aubert, a very careful worker, would have noted reactions in his investigation when he injected large amounts of A and B serum into type O recipients.

Even if A or B plasma obtained from 1 individual might cause reactions because of A or B agglutinogens in solution, it does not follow at all that pooled plasma or serum will result in reactions for the same cause. Aubert's evidence suggests that the A and B substances are suppressed or neutralized in pooling, just as the agglutinins are. In fact, it is scarcely conceivable that A or B agglutinogens can be present free in pooled plasma or serum which certainly contain free agglutinins, even though of a low titer. It is, of course, important that an investigation of the neutralization of these agglutinogens in pooled plasma or serum must be carried out as soon as possible.

Even if it is demonstrated that plasma from 1 individual might have certain elements of danger under some circumstances, this is not at all relevant as far as the use of pooled plasma and serum is concerned.

It is fortunate that Aubert's evidence has called attention to the possible minor risks from the injection of large amounts of incompatible high titered agglutinins, but, as he himself concludes, and as my own evidence also indicates, reactions that might be caused by high titered incompatible agglutinins are not serious and the intravenous administration of pooled plasmas and serums containing low titered incompatible agglutinins are completely safe and without any danger to the patient receiving them.

Nevertheless it is important to investigate whether A and B agglutinogens are neutralized in the process of pooling, and it might be advisable to determine whether the titer of agglutinins in all pools of plasma or serum is not higher than 1:60.

This leads to the suggestion that it seems advisable to have a central authority decide on a standard technic for determining agglutinin titers, since the diversity of technics used by various workers is so great that it is impossible to make any accurate comparison of their results.

CONCLUSION

The extensive clinical evidence and the data which have been analyzed here demonstrate that in pools of a sufficient number of samples of plasma or serum obtained from donors belonging to all four blood groups the titer of both anti A and anti B agglutinins is reduced to such a low level that no danger can result to patients from the injection intravenously of even large therapeutic doses of these pools.

Fifteenth Street and East River.

VITAMINS FOR THE PREVENTION OF COLDS

DONALD W. COWAN, M.D.
HAROLD S. DIEHL, M.D.
AND
A. B. BAKER, M.D.
MINNEAPOLIS

Repeated studies have shown that both animals and man have a decreased resistance to infections of various kinds when suffering from vitamin deficiencies. Apparently this may be true for each of the better known vitamins. On the other hand, it has not been shown by adequately controlled experiments that the addition of any of the vitamins to a reasonably adequate diet produces increased resistance to infections of the upper respiratory tract, the millions of dollars' worth of vitamin preparations which are sold each year for this alleged purpose notwithstanding.

Most of the studies of vitamins for the prevention of colds have been limited to vitamin A alone or to vitamins A and D as contained in cod liver oil. The experiments with vitamin A have resulted almost uniformly in negative results, while cod liver oil has been reported by a number of authors to reduce the severity and by some the frequency of colds. Most of the latter reports, however, are based on inadequately controlled studies.[1]

Investigations of the use of multiple vitamins in the prevention of colds have been very few. Stone and her co-workers [2] reported that the daily administration of concentrates of vitamins A, B_1, B_2 and D were effective in reducing the incidence of infection of the upper respiratory tract in 11 students. These few subjects however, were in poor general physical condition, in addition to being very susceptible to colds, and the observations extended only over a period of three and one-half months.

Kuttner [3] studied 108 rheumatic children in a domiciliary institution. All these children were on the regular institutional diet, but one half of them received each day, in addition to the regular diet, 15,000 U. S. P. units of vitamin A, 1,870 U. S. P. units of vitamin D, 2,000 international units of vitamin C, 1,000 international units of vitamin B_1, 480 Sherman-Bourquin units of vitamin B_2, 40 "rat day" units of vitamin B_6, approximately 40 growth units of "filtrate factor" and the equivalent of 50 Gm. of whole liver in nicotinic acid or one of its derivatives. Both groups were observed from January 1 to June 1, 1939 and from Dec. 1, 1939 to May 1, 1940. The conclusion of the author was that this study did not present any evidence that the addition of these vitamins to an ordinary, well balanced diet reduced the incidence of infections of the upper respiratory tract.

From the Students' Health Service, University of Minnesota.

Read before the Section on Preventive and Industrial Medicine and Public Health at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

1. These include:
Hess, A. F.; Lewis, J. M., and Barenberg, L. H.: Does Our Dietary Require Vitamin A Supplement? J. A. M. A. **101**: 657 (Aug. 26) 1933.
Tress, Esther M.: Vitamin A as a Prophylactic Against the Common Cold in Groups of School Children, Am. J. Digest. Dis. & Nutrition **1**: 795 (Jan.) 1935.
Holmes, A. D.; Pigott, Madeline G.; Sawyer, W. A., and Comstock, Laura: Cod Liver Oil: A Five Year Study of Its Value for Reducing Industrial Absenteeism Caused by Colds and Respiratory Diseases, Indust. Med. **5**: 359 (July) 1936.
Sherman, J. B.: Prophylaxis of the Common Cold, Brit. M. J. **2**: 903 (Oct. 29) 1938.
Spiesman, I. G.: Massive Doses of Vitamins A and D in the Prevention of the Common Cold, Arch. Otolaryn. **34**: 787 (Oct.) 1941.

2. Stone, Florence G.; Bird, Mira S., and Field, Hazel E.: Vitamins A, B_1, B_2 and D: Effects of Daily Administration of Concentrates, California & West. Med. **50**: 125 (Feb.) 1939.

3. Kuttner, A. G.: The Effect of Large Doses of Vitamins A, B, C and D on the Incidence of Upper Respiratory Infections in a Group of Rheumatic Children, J. Clin. Investigation **19**: 809 (Nov.) 1940.

OUTLINE OF STUDY

The present investigation concerns the value of large doses of vitamin C alone (1939-1940 series) and of large doses of mixed vitamins (1940-1941 series) in the prevention of colds. As in our previous cold prevention studies, the subjects were all students of the University of Minnesota who volunteered to participate in the study because they were particularly susceptible to colds.

Students applied for admission to the "Cold Prevention Group" soon after school started in the fall quarter. At this time a record was made of each applicant's recent history of acute infections of the upper part of the respiratory tract with particular attention to the number and severity of colds experienced during the previous two years, the type of these colds, their duration and like information. In order to exclude from the study persons whose difficulties seemed to be due primarily to chronic sinusitis or allergic rhinitis, special attention was paid to the condition of the nose and throat and to symptoms suggestive of allergy. As in previous studies, the students were assigned alternately and without selection to an experimental and to a control group. The students in the control group were treated exactly like those in the experimental groups except that they received placebos instead of the vitamin preparations.

Name _____

Report for week beginning Sunday, _____ (date)

Cold: Date of onset: _____

Continued from previous week. ☐ yes. ☐ no.

Days of cold this week: _____

Severity: ☐ mild; ☐ moderately severe; ☐ severe; ☐ very severe

Symptoms: ☐ nasal discharge ☐ sputum ☐ aching
☐ nasal obstruction ☐ sore throat ☐ in bed
☐ cough ☐ fever Other _____

Medicine: Treatment other than the vaccine taken: _____

Have you taken cold prevention medication daily? ☐ yes. ☐ no.

Reactions: _____

Comments: _____

If, during the week here reported, you have just recovered from a cold, indicate whether that cold as compared with your colds in previous years was AS A WHOLE

☐ very much milder ☐ somewhat milder ☐ very much more severe than average
☐ about the same ☐ more severe

☐ Check here if you have had no symptoms of a cold this week.

(This card must be returned promptly whether you have had a cold or not)

Date of report _____ Signature _____

Fig. 1.—Weekly report card. (The original cards measure 4 by 6 inches.)

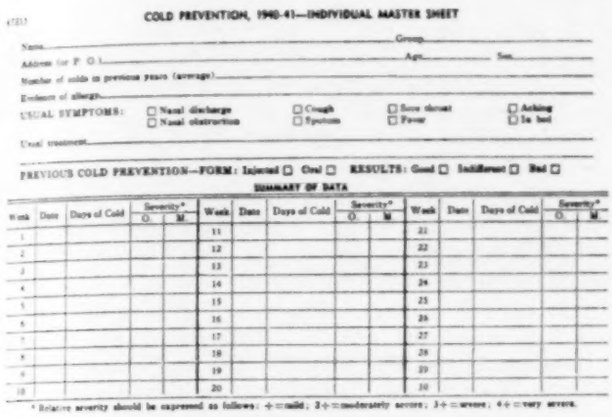
THE REPORTING OF COLDS

The students in all groups were instructed to report to the Health Service whenever a cold developed so that a special report card could be filled in by a physician indicating the type of cold, the symptoms and the like. In addition, all students were interviewed every three months in order to check the completeness of the reports filled out at the time of each respiratory infection.

During the second year of the study (1940-1941) a supplementary check on the accuracy of reporting was instituted. This consisted in having each student fill out and return to the Health Service each week the special report card shown in figure 1. This card is

similar to the one used by Stafford [4] and provides an accurate check on the incidence of colds as well as some information as to the relative severity of each cold reported.

The data contained on these weekly report cards were transferred to each student's "master card," which was



COLD PREVENTION, 1940-41—INDIVIDUAL MASTER SHEET

Name _____ Group _____

Address (or P. O.) _____ Age _____ Sex _____

Number of colds in previous years (average) _____

Evidence of allergy _____

USUAL SYMPTOMS: ☐ Nasal discharge ☐ Nasal obstruction ☐ Cough ☐ Sputum ☐ Sore throat ☐ Fever ☐ Aching ☐ In bed

Usual treatment _____

PREVIOUS COLD PREVENTION—FORM: Injected ☐ Oral ☐ RESULTS: Good ☐ Indifferent ☐ Bad ☐

SUMMARY OF DATA

Week	Date	Days of Cold	Severity* O	Severity* M	Week	Date	Days of Cold	Severity* O	Severity* M	Week	Date	Days of Cold	Severity* O	Severity* M
1					11					21				
2					12					22				
3					13					23				
4					14					24				
5					15					25				
6					16					26				
7					17					27				
8					18					28				
9					19					29				
10					20					30				

* Relative severity should be expressed as follows: + = mild; 2+ = moderately severe; 3+ = severe; 4+ = very severe.

Fig. 2.—Master card.

kept on file in the Health Service (fig. 2). At the end of the school year these various reports were summarized according to experimental and control groups.

DAILY USE OF LARGE DOSES OF VITAMIN C

At the beginning of the school year 1939-1940, 427 were enrolled in the "cold prevention group." One hundred and eighty-three of these were supplied with 100 mg. tablets of synthetic ascorbic acid and were instructed to take 2 such tablets (200 mg.) daily throughout the "cold season," a total of twenty-eight weeks. Fifty other students, also supplied with 100 mg. tablets of ascorbic acid, were instructed to take 2 tablets (200 mg.) daily for the first two weeks, then 1 tablet (100 mg.) daily throughout the season unless and until an infection of the upper respiratory tract developed, in which case they were to take 5 tablets (500 mg.) on each of the first two days of the cold, after which the 100 mg. daily dose was to be resumed. Since the results of these two subgroups were not significantly different, they are presented in table 1 as a single vitamin C group.

TABLE 1.—*Vitamin C in the Prevention of Colds*

	Vitamin C Group	Control Group
Subjects who began study	233	194
Subjects who completed study	208	155
Percentage who completed study	89.3	79.9
Number of colds per person during previous year* (average)	5.5 ± 0.12	5.9 ± 0.14
Number of colds per person during year of study (average)	1.9 ± 0.07	2.2 ± 0.08
Difference between average number of colds in experimental and control groups	0.3 ± 0.11	
Percentage of group who had no colds during year	11.5	8.4
Number of days per person lost from school (average)	1.1	1.6
Percentage of students with colds in which complications developed	26.4	22.6
Percentage of group reporting such reactions as headache, nausea, hot flashes and so on	4.8	1.3

* Reported from memory.

To serve as a control group 194 students were supplied with placebo tablets of the same size, shape, appearance and taste as the ascorbic acid tablets.[5] These students, of course, did not know that they were serving as controls. The instructions were to take 2 of these placebo tablets daily throughout the "cold season."

It will be noted that, while the students who took vitamin C throughout the "cold season" experienced only 1.9 colds per person annually during the study as compared with the reported 5.5 colds per person annually previous to the study, a reduction of 65.5 per cent, the controls reported an average of 2.2 colds per person a year during the study as compared with 5.9 colds per person annually in previous years, a reduction nearly as great, namely 62.7 per cent. The actual difference between the two groups during the year of the study amounts to one third of a cold per person. Statistical analysis of the data reveals that a difference as large as this would arise only three or four times in a hundred through chance alone. One may therefore consider this as probably a significant difference, and vitamin C supplement to the diet may therefore be judged to give a slight advantage in reducing the number of colds experienced. However, one may well

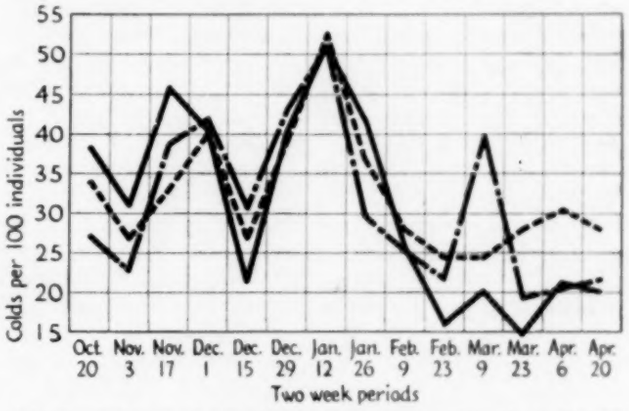


Fig. 3.—Incidence of colds in three groups of students from Oct. 20, 1940 to April 20, 1941. Broken line indicates group given 2 multiple vitamin capsules daily; dot and dash line indicates group given 1 multiple vitamin capsule plus added thiamine hydrochloride and nicotinic acid daily, and solid line indicates control group given 2 placebo capsules daily.

question the practical importance of such a difference. There are also slight differences in favor of the vitamin C group in regard to the percentage of students who had no colds of twenty-four or more hours' duration during the year of the study and in regard to the average number of days lost from school because of colds. On the other hand, those who took the vitamin C had, if anything, more complications such as bronchitis, otitis and sinusitis than did those in the control group.

MULTIPLE VITAMINS IN COLD PREVENTION

At the beginning of the school year 1940-1941 a total of 347 students were enrolled in the multiple vitamin study. Of this group only 264 cooperated throughout the year, which represents a smaller percentage than in most of our studies, possibly because of the increased demand made on the students during this year in the form of weekly report cards, special examinations of the nose and throat and the like. The results shown in figure 3 and table 2 are based only on those who cooperated throughout the "cold season."

At the beginning of the year 120 of these 347 students were instructed to take 2 capsules of multiple vitamins ("Hepicebrin") daily throughout the "cold season."

4. Stafford, C. I.: The Common Cold: An Evaluation of an Oral Vaccine Based on a Controlled Study, Journal-Lancet **60**: 319 (July) 1940.

5. Both the ascorbic acid and the placebo tablets were furnished by Hoffmann-LaRoche, Inc., Nutley, N. J.

These provided a daily supplement of 20,000 U. S. P. units of vitamin A, 1.2 mg. of thiamine hydrochloride, 200 micrograms of riboflavin, 50 mg. of ascorbic acid and 2,000 U. S. P. units of vitamin D. A second group of 107 students was given the following daily vitamin supplements: vitamin A 10,000 U. S. P. units, thiamine hydrochloride 48.6 mg. daily for the first week and 3.6 mg. daily thereafter, riboflavin 100 micrograms, ascorbic acid 25 mg., vitamin D 1,000 U. S. P. units and after January 1 nicotinic acid 50 mg. daily. This dosage was obtained by the daily administration of 1 multiple vitamin capsule together with the thiamine hydrochloride and nicotinic acid already indicated.

The control group for the experiment consisted of 120 students who were furnished placebo capsules which were indistinguishable from the multiple vitamin capsules.[6] These were prescribed at the rate of 2 daily throughout the "cold season."

TABLE 2.—*Multiple Vitamins in the Prevention of Colds*

	Two Multiple Vitamin Capsules Daily	One Multiple Vitamin Capsule + Thiamine + Nicotinic Acid Daily	Control (Two Capsules Placebo Daily)
Subjects who began study	120	107	120
Subjects who completed study	82	88	94
Percentage who completed study	68.3	82.2	78.3
Number of colds per person during previous year * (average)	4.9	5.0	5.0
Number of colds per person during year of study (average)	2.4	2.4	2.4
Percentage of group with no colds during year	4.9	8.0	5.3
Number of days per person lost from school (average)	1.8	1.6	1.0
Percentage of students with colds in which complications developed	23.5	15.2	13.5
Percentage of students hospitalized with complications	2.5	5.1	1.1
Classification of colds experienced (percentage of total colds in group):			
1. Based on symptomatology: †			
Mild	73.2	73.8	72.2
Moderately severe	14.1	14.8	16.6
Severe	9.6	8.1	7.6
Very severe	3.0	3.3	3.6
2. Based on student's opinion as to comparison with previous colds: †			
Very much milder than average previous cold	28.3	28.2	22.6
Somewhat milder than average previous cold	31.2	22.4	25.0
About the same as average previous cold	28.9	34.0	36.9
More severe than average previous cold	9.8	10.9	8.9
Very much more severe than average	1.7	4.5	6.5
3. Average duration of colds, days	8.2	8.0	8.1

* Reported from memory.
† Classifications explained in text.

RESULTS WITH MULTIPLE VITAMINS

Table 2 and figure 3 present the results of this study. From table 2 it is apparent that there is no difference in the number of colds reported by the experimental and control groups. The same is true for the weekly occurrence of colds as shown in figure 3. The total number of colds reported by students in all groups was higher in this study than in most of our other experiments. This is in keeping with the general impression that the year 1940-1941 was characterized by an exceptionally high incidence of colds in the general school population.

Table 2 also presents an attempt to evaluate the relative severity of the colds reported by the students in the various groups. Three sets of criteria were used in this analysis. The severity of colds as reported on the weekly cards was estimated in much the same manner as was utilized by Shibley and Spies [7] and by Stafford.[4] The occurrence of nasal discharge and obstruction with or without cough, sputum or sore throat lasting for more than one day but without aching, fever or confinement to bed was classified as a mild cold. The presence in addition of one of the recorded features of fever, aching or confinement to bed resulted in the classification moderately severe; if two of these features were present the cold was labeled severe, and if all three were present, that is if the student reported that he had fever, generalized aching and was confined to bed, the cold was classified as very severe.

In a further attempt to determine whether the medication modified the severity of the colds, the student was asked at the end of each cold he did experience to give an opinion as to how that particular cold compared with his previous colds (fig. 1).

An examination of table 2 does not reveal any evidence that the multiple vitamins reduced the severity of the colds. In fact, complications were more frequent among the students who got the vitamin supplements than among the control group. Furthermore, the average duration of each cold was the same for all three groups.

SUMMARY

This controlled study yields no indication that either large doses of vitamin C alone or large doses of vitamins A, B_1, B_2, C and D and nicotinic acid have any important effect on the number or severity of infections of the upper respiratory tract when administered to young adults who presumably are already on a reasonably adequate diet.

ABSTRACT OF DISCUSSION

DR. JOHN A. FERRELL, New York: May I inquire of the authors whether some of their study and control groups were known to have one or more vitamin deficiencies when the observations began? If not, what would be the rationale of administering vitamins to persons among whom no deficiencies had been determined with a view of influencing the incidence of colds due to viruses? With regard to the influenza viruses, the authorities in this field report that when resistance is built up against a specific virus the antibody titer for this virus is raised to a notable degree. Did you make any tests of your subjects relative to their antibody status for one or another of the viruses? The answers to these questions would be of real importance when testing the effectiveness of any therapeutic agent against a specific infection.

DR. JOSEPH S. LAWRENCE, Albany, N. Y.: Although the figures show practically no difference in the prevalence of colds between the two groups, if I gathered correctly from the statistics, there was, however, an appreciable diminution of colds among those examined as compared with the prevalence of colds among other students that winter. The students of both groups claimed also that they had had fewer colds than in the preceding winter. I wonder if the authors of the paper have an explanation for this apparent difference in incidence.

DR. HAVEN EMERSON, New York: This is a matter of the greatest importance to officers of the government concerned with the character of advertising claims that certain commercial preparations will stop and cure colds. The whole technic of

6. The vitamins as well as the placebo capsules were furnished by Eli Lilly & Co., Indianapolis.

7. Shibley, G. S., and Spies, T. D.: The Effect of Vitamin A on the Common Cold, J. A. M. A. **103:** 2021 (Dec. 29) 1934.

testing colds is at stake, and this is a good example of a carefully controlled study. I hope other questions as pointed as those that have been asked will be put to the authors. This is not an isolated undertaking in clinical research. Dr. Diehl and his colleagues have made many efforts to unravel the epidemiology of colds and to produce some practical proof of prevention and of successful treatment.

DR. DONALD W. COWAN, Minneapolis: In regard to the first question, we did no analyses to see whether or not the students were suffering from vitamin deficiency. We assumed that they were not, since most of them were on a reasonably adequate diet. We made no antibody studies either. We had no preconceived idea as to the value of vitamin therapy in the reduction of colds. We didn't know whether they would help or would not help. We merely used the vitamins because so many of them were being used by so many people that we thought a real controlled study was indicated to determine whether or not there might be something to the belief that persons taking large doses of expensive vitamins had fewer colds. There is, as far as I know, no rationale for it, and we certainly were not able to demonstrate that the vitamins were of any value. In regard to the question asked by Dr. Lawrence, there is a remarkable decrease in the reported number of colds on the part of both the control subjects and the experimental subjects in all of our cold prevention studies. We are at a loss to explain this 60 to 65 per cent reduction that we find in persons who are taking injections of sterile saline solution when they are controlling an experiment with injected vaccine, or starch tablets when they are controlling some oral vaccine, or capsules of liquid petrolatum when they are acting as controls for vitamin concentrates. One thing that might enter into the remarkable reduction in the number of colds among students in the control group is the fact that when one is taking two or three pills every day or is given a shot in the arm once or twice a week because he is cold susceptible he is continually being reminded that he is trying to do something about his colds; and he might consciously or unconsciously practice better general hygiene, which might decrease the number of colds which he has. For example, at Minnesota students are often observed dashing from their rooming houses to the corner drug store at 20 below zero without hats or coats. I wonder whether they aren't more likely to put on a hat and coat when they are in the cold prevention group.

DR. HAROLD S. DIEHL, Minneapolis: In further response to Dr. Ferrell's question, the reason for making this study was not that we thought these students exhibited vitamin deficiencies but that the average population is buying millions of dollars' worth of these vitamins every year, much of which is stimulated by advertising which suggests that vitamins will prevent colds. The question that we were attempting to answer was Are vitamins of any value for the prevention of colds in a cross section of the population such as we get in a university? In a group of university students one would not expect to find much vitamin deficiency, and yet in a big state university, such as Minnesota, a large portion of our students are self supporting, living in rooming houses and eating in restaurants. Observing cafeteria selections, we know their diets are not what we would recommend. Hence we can be certain that the economic level of these students and the type of diet they are getting is probably not as good as that of the average person who buys vitamin pills. Another point emphasized by this study, as well as by our previous studies on colds, is that if studies of this sort are to have any significance they must be done with a control group, and that control group must be treated in the same way as the experimental group. Results are not significant if this control group receives nothing. The control group must be given something which has the same psychologic effect as the treatment received by the experimental group. Our studies show that placebos frequently give what appear to be excellent results. It is common for the control group to report a reduction from an average of five to about two colds a year. In fact, certain results reported by many persons who received placebos would serve as splendid testimonials for anything for the prevention of colds.

CARDIAC EFFICIENCY AND PROGNOSIS FOLLOWING RECOVERY FROM ACUTE CORONARY OCCLUSION

THE RESULTS OF VARIOUS FUNCTIONAL TESTS

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Medical Corps, United States Naval Reserve
SIMON DACK, M.D.
AND
HARRY L. JAFFE, M.D.
NEW YORK

In previous reports we [1] presented detailed clinical observations of 202 patients with acute coronary occlusion followed for a period of one to seven years after discharge from the hospital. Particular attention was paid to the cardiac status as determined by symptoms and physical examination. It was found that at least one third of the patients were able to lead a fairly active life with little or no restriction of ordinary activities and one half were able to return to full or part time work.

This study represents the results of objective tests of cardiac function performed serially in these 202 patients now followed two to eight years. These tests were vital capacity, the "Master two step" exercise tolerance, teleoroentgenogram for the size and configuration of the heart, fluoroscopic and roentgenkymographic study of ventricular pulsation, ordinary electrocardiogram and electrocardiogram after the standard "two step" exercise. An attempt was made to correlate the results of the tests with the clinical symptoms, physical findings and subsequent course of the patient. By repetition of the tests at intervals of three to twelve months it was possible to determine approximately when each test returned to normal.

To evaluate the various tests, the patients were grouped according to the degree of recovery. This was based on the presence and severity of angina pectoris, dyspnea and weakness and the physical findings, such as heart size, heart sounds and rate, signs of heart failure and blood pressure. Recovery of 66 patients (33 per cent) was considered good, of 57 (28 per cent) fair and of 79 (39 per cent) poor.

VITAL CAPACITY

Peabody and Wentworth,[2] Pratt [3] and subsequently other investigators [4] demonstrated a close relationship between a decreased vital capacity and pulmonary congestion due to left ventricular failure. White and

From the Mount Sinai Hospital.

Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the authors' reprints.

Read before the joint meeting of the Section on Practice of Medicine and the Section on Experimental Medicine and Therapeutics at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1942.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth in this article are those of the writers and are not to be considered as reflecting the policies of the Navy Department.

1. Master, A. M., and Dack, Simon: Rehabilitation Following Acute Coronary Occlusion, J. A. M. A. **115:** 828-832 (Sept. 7) 1940. Master, Dack and Jaffe.[10]

2. Peabody, F. W., and Wentworth, J. A.: Clinical Studies on Respiration: IV. The Vital Capacity of the Lungs and Its Relation to Dyspnea, Arch. Int. Med. **20:** 443-467 (Sept.) 1917.

3. Pratt, J. H.: Long Continued Observations on the Vital Capacity in Health and Heart Disease, Am. J. M. Sc. **164:** 819-836 (Dec.) 1922.

4. Harrison, T. R.; Turley, F. C.; Jones, Edgar, and Calhoun, J. A.: Congestive Heart Failure: X. The Measurement of Ventilation as a Test of Cardiac Function, Arch. Int. Med. **48:** 377-398 (Sept.) 1931. Robb, G. P., and Weiss, Soma: The Velocity of Pulmonary and Peripheral Venous Blood Flow and Related Aspects of the Circulation in Cardiovascular Disease: Their Relation to Clinical Types of Circulatory Failure, Am. Heart J. **9:** 742-763 (Aug.) 1934.

McGinn [5] reemphasized the value of the vital capacity as a measure of pulmonary congestion, particularly when repeated determinations were made on the same patient.

In a previous study [6] of acute coronary occlusion, serial determinations of the vital capacity during the acute stage revealed a moderate to pronounced reduction (400 to 2,000 cc.) in two fifths of 80 patients. With clinical improvement the vital capacity tended to rise progressively.

TABLE 1.—*Vital Capacity*

Normal (3,000 cc. or more)	72	(38%)
Slightly diminished (2,500 to 3,000 cc.)	52	(27%)
Moderately diminished (2,000 to 2,500 cc.)	49	(26%)
Considerably diminished (less than 2,000 cc.)	16	(8.5%)
Not done	13	
	202	

The present follow-up study contains repeated vital capacity determinations on 189 patients (table 1). One third had a vital capacity of 2,500 cc. or less, representing a moderate to pronounced reduction from normal. A return to normal occurred generally during the first year after the attack and in more than half the patients within five months (table 7).

The small incidence of very low vital capacity (8.5 per cent) conforms with the infrequency of chronic heart failure and severe dyspnea in our series. As might be expected, the lowest vital capacity readings were encountered in the poor recovery group (table 8), but even in this group the vital capacity not infrequently was normal when heart failure was absent, the disability being due to angina pectoris. Therefore a normal vital capacity does not exclude the presence of cardiac disability, although a significant degree of heart failure is unlikely.

EXERCISE TOLERANCE TEST

Numerous types of exercise tolerance tests have been advocated for the determination of cardiac function. While no test is wholly free from criticism, we have found the Master two step test [7] simple and reliable. The test is based on the effect on the pulse rate and blood pressure of walking up and down two steps, each

TABLE 2.—*Two Step Exercise Tolerance Test*

Normal tolerance	34	(18%)
Upper limit of normal or slightly abnormal	31	(17%)
Definitely abnormal	119	(65%)
Test not performed	18	
	202	
Pain, dyspnea, fatigue after test	114	(62%)
No symptoms after test	70	(38%)

9 inches in height. The total number of climbs required of each subject is determined from prepared tables [7] based on sex, age and weight and is performed in one and one-half minutes. The pulse rate and blood pressure normally return to within 10 points of resting levels within two minutes after the exercise.

This test is particularly suitable for patients with coronary artery disease and angina pectoris because of the short duration and nonstrenuous nature of the exercise and because the amount of exercise necessary to produce symptoms of coronary insufficiency, such as pain, dyspnea and fatigue, can be determined. This is of great aid in studying the progress of the patient [8] and the degree of myocardial reserve. In recent years we have combined the two step test with the electrocardiogram, recording the latter before and immediately after exercise.[9]

The exercise tolerance was performed serially by 178 patients (table 2). The response of the pulse rate and blood pressure was normal in 18 per cent of the patients and distinctly abnormal in almost two thirds. The majority of the latter complained of pain, dyspnea or undue fatigue during or immediately after the test.

The exercise tolerance test usually did not return to normal until one or two years after the attack (table 7). In a few cases the return to normal occurred as early as two to five months after the attack and in a small group only after three or four years. Return of the exercise tolerance to normal was usually associated with a good recovery from the attack. Although 42 per cent of the good recovery group responded abnormally to this test, the frequency of an abnormal response was much higher (86 per cent) in the poor recovery group (table 8).

TABLE 3.—*Heart Size (Teleoroentgenogram and Fluoroscopy)*

Normal size		64	(32.5%)
Normal size with left ventricle hypertrophy		10	(16.5%)
Slight or borderline enlargement		22	
Definite enlargement		100	(51%)
1 plus enlargement	36		
2 plus enlargement	47		
3 plus enlargement	13		
4 plus enlargement	4		
Not determined		6	
		202	

HEART SIZE (TELEOROENTGENOGRAM)

The relation of coronary sclerosis, coronary occlusion and myocardial infarction to cardiac enlargement has been the subject of numerous clinical and pathologic studies. Several investigators [10] believe that coronary sclerosis or myocardial infarction is often the sole factor in the development of cardiac enlargement. The preponderant opinion,[11] however, is that coronary disease or myocardial infarction as such does not lead to ventricular enlargement unless hypertension has been present or congestive heart failure intervenes. Our observations [12] during the acute attack have shown that approximately three fifths of cases give evidence of cardiac enlargement, particularly of the left ventricle.

5. White, P. D., and McGinn, Sylvester: The Importance of the Clinical Recognition of Weakness and Failure of the Left Ventricle Without Failure of the Right Ventricle, Tr. A. Am. Physicians **48:** 104-120, 1933.

6. Master, A. M.; Dack, Simon, and Jaffe, H. L.: Coronary Thrombosis: An Investigation of Heart Failure and Other Factors in Its Course and Prognosis, Am. Heart J. **13:** 330-361 (March) 1937.

7. Master, A. M., and Oppenheimer, Enid T.: A Simple Exercise Tolerance Test for Circulatory Efficiency with Standard Tables for Normal Individuals, Am. J. M. Sc. **177:** 223-242 (Feb.) 1929. Master.[23]

8. Riseman, J. E. F., and Stern, Beatrice: A Standardized Exercise Tolerance Test for Patients with Angina Pectoris on Exertion, Am. J. M. Sc. **188:** 644-659 (Nov.) 1934.

9. Master, A. M.; Friedman, R., and Dack, Simon: The Electrocardiogram Following Standard Exercise as a Functional Test of the Heart, to be published. Master.[25]

10. Bartels, E. C., and Smith, H. L.: Gross Cardiac Hypertrophy in Myocardial Infarction, Am. J. M. Sc. **184:** 452-455 (Oct.) 1932. Willius, F. A.: Cardiac Clinics: Clinic on Angina Pectoris with Coronary Sclerosis; Previous Coronary Thrombosis with Healed Cardiac Infarction, Proc. Staff Meet., Mayo Clin. **10:**234-239 (April 10) 1935.

11. Nathanson, M. H.: Disease of the Coronary Arteries: Clinical and Pathological Features, Am. J. M. Sc. **170:** 240-255 (Aug.) 1925. Miller, H. R., and Weiss, M. M.: Disease of Coronary Arteries: Its Occurrence Without Gross Cardiac Hypertrophy, Arch. Int. Med. **42:** 74-78 (July) 1928. Appelbaum, Emanuel, and Nicolson, Gertrude H. B.: Occlusive Diseases of the Coronary Arteries: An Analysis of the Pathological Anatomy in 168 Cases, with Electrocardiographic Correlation in 36 of These, Am. Heart J. **10:** 662-680 (June) 1935. Horine and Weiss.[13] Palmer.[14]

12. Master, A. M.; Dack, Simon, and Jaffe, H. L.: Age, Sex and Hypertension in Myocardial Infarction Due to Coronary Occlusion, Arch. Int. Med. **64:** 767-786 (Oct.) 1939. Master, Dack and Jaffe.[9]

The vast majority of these are hypertensive or give a history of previous hypertension.

Similar findings have been reported during the follow-up period. In a radiologic study of 20 cases of coronary occlusion with normal heart size followed one half to ten years, Horine and Weiss [13] found no increase in heart size, suggesting that enlargement does not occur unless hypertension or heart failure has been present. Palmer [14] found distinct cardiac enlargement radiographically in 64 per cent of 200 patients who had survived a coronary occlusion at least three months and considered hypertension the causative factor in four fifths.

In the present study serial teleoroentgenograms were obtained in 196 cases (table 3). About one half had definite enlargement, graded 1 to 4 plus; in one third the heart size was within normal limits and in the remainder left ventricular hypertrophy with little or no gross enlargement of the heart was present.

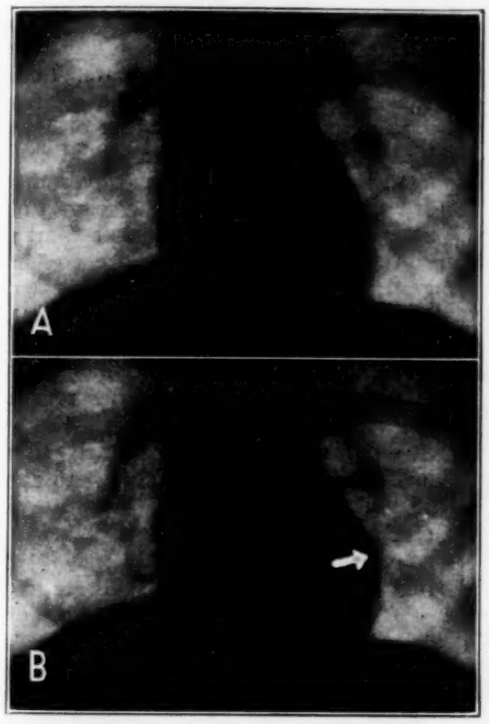

Fig. 1.—Cineroentgenograms (movies of fluoroscopic screen) of a man aged 44 who sustained a coronary occlusion two months before. *A*, diastole; *B*, systole. A localized expansion of the midportion of the left ventricle is observed during systole (arrow). This is characteristic of previous infarction. The electrocardiogram, which showed inversion of T_2 and T_3 during the acute attack, returned to normal within two months, at the time of this fluoroscopic examination.

It has previously been pointed out [15] that hypertension (150 mm. or more systolic and 90 mm. or more diastolic) had been known to exist in 60.4 per cent of the patients prior to the acute attack of coronary occlusion. During the follow-up period the incidence of hypertension was only 37.8 per cent, indicating that in over one third of hypertensive patients the blood pressure failed to regain a hypertensive level.

Cardiac enlargement was observed in only one third of the good recovery group but in over two thirds of those making a poor recovery (table 8). Thus, recovery of cardiac function is more apt to be complete when the heart size is normal; yet a severe degree of coronary disease may exist without cardiac enlargement. In such a case disability is usually due to angina pectoris rather than to heart failure.

TABLE 4.—*Ventricular Pulsations (Roentgenkymogram and Fluoroscopy)*

Normal pulsation		22	(12.3%)
Slight diminution (not abnormal)		8	(4.3%)
Definite impairment of pulsation		146	(83.0%)
Moderate or considerable diminution	32 (18%)		
Absence of pulsation	12 (7%)		
Reversal of pulsation	102 (58%)		
Partial	30		
Complete	72		
Not examined		26	
		202	

VENTRICULAR PULSATIONS (FLUOROSCOPY AND ROENTGENOGRAM)

Myocardial infarction following acute coronary occlusion can be detected fluoroscopically in half the cases by the presence of localized systolic expansion or reversal of pulsation of the left ventricular border.[16] Instead of a unform contraction of the left ventricle a lateral movement is observed during systole, usually in its lower half (fig. 1). Furthermore, 20 per cent of cases exhibit other abnormalities of contraction, such as localized absence or diminution of left ventricular pulsation. In the remaining cases the ventricular pulsations remain normal. These fluoroscopic observations have been confirmed by roentgenkymographic studies.[17]

In the present series repeated observations of the ventricular pulsations were made fluoroscopically or kymographically on 176 patients (table 4). In 58 per cent the findings were characteristic of infarction, that is, complete or partial systolic expansion was present; nonspecific changes, i. e. absent or diminished pulsations, were present in 25 per cent. Therefore normal pulsations existed in only 30 cases, or 17 per cent. As a rule the abnormality observed during the acute attack persisted or changed slightly in degree. In only 19 cases did an abnormal type of pulsation disappear in serial

TABLE 5.—*Electrocardiographic Findings*

Normal		28	(21%)
Slightly abnormal		15	
Abnormal		33	(16%)
Not specific	11		
Hypertensive record	15		
Intraventricular block	7		
Anterior pattern		70	(35%)
(Q-1-4 alone)	4		
(Q-4 alone)	5		
(Q-4 T-4 alone)	2		
Posterior pattern		27	(13%)
(Q-3 alone)	1		
Anterior-posterior pattern		29	(14%)
(Q-1-2-3 alone)	2		
		202	

13. Horine, E. F., and Weiss, M. M.: Coronary Thrombosis and Its Effect on the Size of the Heart, Am. J. M. Sc. **189:** 858-860 (June) 1935.

14. Palmer, J. H.: The Size of the Heart After Coronary Thrombosis, Canad. M. A. J. **36:** 387-392 (April) 1937.

15. Master, A. M.; Dack, Simon, and Jaffe, H. L.: Follow-Up Studies in Coronary Artery Occlusion: I. Degree of Recovery, Symptoms and Physical Signs, New York State J. Med. **42:** 413-420 (March 1) 1942.

16. Master, A. M.; Gubner, Richard; Dack, Simon, and Jaffe, H. L.: The Diagnosis of Coronary Occlusion and Myocardial Infarction by Fluoroscopic Examination, Am. Heart J. **20:** 475-485 (Oct.) 1940. Master, A. M.: Roentgenoscopy as a Diagnostic Aid in Coronary Occlusion: A Study of 164 Cases, Am. J. Roentgenol. **45:** 350-356 (March) 1941.

17. Gubner, Richard, and Crawford, J. H.: Roentgenkymographic Studies of Myocardial Infarction, Am. Heart J. **18:** 8-24 (July) 1939. Sussman, M. L.; Dack, Simon, and Master, A. M.: The Roentgenkymogram in Myocardial Infarction: I. The Abnormalities in Left Ventricular Contraction, ibid. **19:** 453-463 (April) 1940.

examinations, usually during the first year and sometimes only after several years (table 7).

The presence of abnormal ventricular contraction did not preclude a good recovery from the acute attack. Thus an abnormal pulsation was observed in 70 per cent of the patients whose clinical recovery was classed as good. Nevertheless the ventricular pulsations are significant in the prognosis, for the incidence of abnormal pulsations was far greater in the poor recovery group, namely 94 per cent (table 8). In general, a patient with normal myocardial contractions makes a good clinical recovery despite the persistence of other abnormal tests. This suggests that normal ventricular contraction following coronary occlusion is associated with a small myocardial infarct or a well healed scar.[18]

A study of ventricular pulsation following coronary occlusion is of diagnostic as well as prognostic value, since systolic expansion may be the only residual pathognomonic sign of previous infarction.[19] This was emphasized in a previous study [20] in which it was found that, although 44 patients presented electrocardiograms

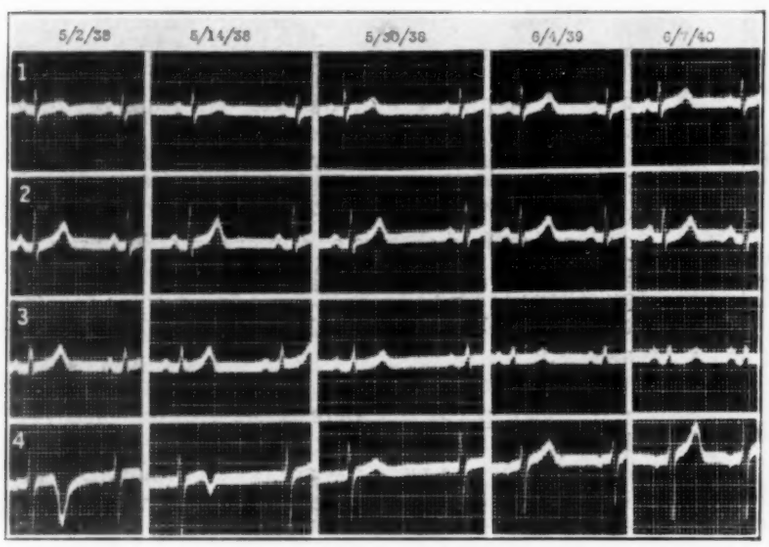

Fig. 2.—Serial electrocardiograms of a man aged 52 who sustained an acute coronary occlusion, April 25, 1938. Partial inversion of T_1 and deep inversion of T_4 indicate anterior wall infarction. The changes are transient. The record five weeks after the attack and subsequent records are normal. Clinical recovery was excellent; symptoms were absent, and all the functional tests became normal. The patient returned to regular, full time work.

which had returned to normal or almost normal, the fluoroscopic or kymographic examination revealed systolic expansion in a majority of them. Similar observations were made in the present series (fig. 1). The ventricular pulsations may be helpful not only when the electrocardiogram has returned to normal but also when it is abnormal but has lost the typical appearance of previous infarction.

ELECTROCARDIOGRAM

In recent years the various electrocardiographic changes occurring during the acute and subacute stages of coronary occlusion have been thoroughly studied.[21] It has been demonstrated that the characteristic Q_1Q_4, T_1T_4 pattern of anterior infarction or the Q_2Q_3, T_2T_3 pattern of posterior infarction develops in the great majority of cases in which serial tracings are obtained and that anterior and posterior infarctions occur with almost equal frequency.[22] In a smaller group of cases the findings of both anterior and posterior infarction are observed and the electrocardiographic pattern may be less characteristic than in the former groups. Rarely the electrocardiogram remains normal in coronary occlusion or shows atypical changes, even in serial records. The observations made on the electrocardiogram during the years following recovery from the attack have not been detailed but it is known that good recovery may take place and yet T wave inversions persist.[23] Marvin [24] observed that the persistence of T wave inversion following recovery did not significantly influence prognosis, since he found that inverted T waves persisted among several patients who were leading active lives, and, on the other hand, the return of the T waves to normal occurred among several patients who subsequently developed severe angina pectoris or heart failure. Levine and Rosenbaum [25] noted that the electrocardiographic pattern, whether that of anterior or that of posterior infarction, did not affect length of survival or frequency and severity of subsequent angina pectoris. Following anterior infarction subsequent heart failure, however, seemed to be more common and restriction of physical activity greater. This was in accord with previous observations of Wood and his associates.[26]

The electrocardiographic findings in serial records obtained in our series of 202 cases are summarized in table 5. The electrocardiogram returned completely to normal in 28 cases (fig. 2) and almost to normal in 15 others. Thus the electrocardiogram returned practically to normal in more than one fifth of the cases, illustrating the fact that the absence of typical electrocardiographic changes does not exclude previous coronary occlusion.[20] The electrocardiogram returned to normal in a variable interval, ranging from less than one month to four years. The majority returned to normal within one year (table 7). In 33 cases the electrocardiogram was abnormal but the typical pattern of myocardial infarction had been lost; 15 of these were of the "hypertensive" type seen in left ventricular enlargement and strain, and in 7 intraventricular block masked the signs of previous infarction.

Changes that were characteristic or suggestive of old infarction persisted in the remaining 126 cases. In 70 the pattern suggested anterior infarction, in 27 posterior infarction and in 29 combined anterior and posterior infarction. Even in these groups a regression

18. Dack, Simon; Sussman, M. L., and Master, A. M.: The Roentgenkymogram in Myocardial Infarction: II. Clinical and Electrocardiographic Correlation, Am. Heart J. **19**: 464-474 (April) 1940.

19. Master, Gubner, Dack and Jaffe.[18] Dack, Sussman and Master.[18]

20. Sussman, M. L., and Dack, Simon: The Roentgenkymogram in Myocardial Infarction. III. Cases with Normal Electrocardiogram, J. Mount Sinai Hosp. **8**: 1064-1070 (Jan.-Feb.) 1942.

21. Parkinson, J., and Bedford, D. E.: Successive Changes in the Electrocardiogram After Cardiac Infarction (Coronary Thrombosis), Heart **14**: 195-239 (Aug.) 1928. Wilson, F. N.; Macleod, A. G.; Barber, P. S.; Johnston, F. D., and Klostermeyer, L. L.: The Electrocardiogram in Myocardial Infarction with Particular Reference to the Initial Deflections of the Ventricular Complex, ibid. **16**: 155-177 (June) 1933. Barnes and Whitten.[22] Wood, Bellet, McMillan and Wolferth.[26]

22. Barnes, A. R., and Whitten, M. B.: Study of the RT Interval in Myocardial Infarction, Am. Heart J. **5**: 142-171 (Dec.) 1929. Master, Dack and Jaffe.[6]

23. Master, A. M.: The Two Step Test of Myocardial Function, Am. Heart J. **10**: 495-510 (April) 1935.

24. Marvin, H. M.: Some Aspects of Cardiovascular Disease, Proceedings of the Twenty-Ninth Annual Meeting of the Medical Section, American Life Insurance Convention, Hot Springs, Va., June 1939.

25. Levine, S. A., and Rosenbaum, F. F.: Prognostic Value of Various Clinical and Electrocardiographic Features of Acute Myocardial Infarction: II. Ultimate Prognosis, Arch. Int. Med. **68**: 1215-1231 (Dec.) 1941.

26. Wood, F. C.; Bellet, Samuel; McMillan, T. M., and Wolferth, C. C.: Electrocardiographic Study of Coronary Occlusion: Further Observations on the Use of Chest Leads, Arch. Int. Med. **52**: 752-784 (Nov.) 1933.

of the abnormalities often occurred. In many cases a T wave which had been abnormal in two or more leads remained abnormal in only one lead. Not infrequently all the T waves returned to normal and only small or deep Q waves persisted (fig. 3). Thus, in the anterior infarction group 4 cases presented only a deep Q_1 and Q_4 and in 5 cases all the changes disappeared except for a persistent deep Q_4; in 2 cases the standard leads returned entirely to normal but the precordial lead still presented the Q_4 T_4 pattern. Similarly, in 1 case of the posterior infarction group all the changes returned to normal except a persistent deep Q_3 (fig. 3), while in 2 cases of the anterior-posterior infarction group all the T waves became normal but the Q waves persisted in the standard leads.

The electrocardiogram became normal in 35 per cent of the good recovery group and in only 3 per cent of the poor recovery group (table 8). Hence return of the electrocardiogram to normal or almost normal was generally, although not invariably, associated with a good prognosis (fig. 2). Furthermore, in the cases mentioned in which the T waves returned to normal and only deep Q waves persisted, a good or fair recovery was the rule. On the other hand, persistence of the characteristic electrocardiographic changes was not necessarily a bad prognostic sign, since this was true of the majority of patients making a good recovery. In our experience, not only is the location of the infarct of little importance with regard to severity and mortality rate of the acute attacks,[6] but it also does not appreciably affect the clinical course during the follow-up period. A good recovery occurred in 33 per cent of patients with a persistent anterior infarction pattern and in 37 per cent of those with signs of a posterior lesion. However, the incidence of good recovery dropped to 22 per cent when signs of both existed. This can be attributed to the fact that the acute infarct was of larger extent or that two separate infarcts occurred. Good recovery was also uncommon, occurring in only 13 per cent in the group of cases in which the electrocardiograms remained abnormal, although not characteristic of previous infarction, including those with a hypertensive pattern or intraventricular block.

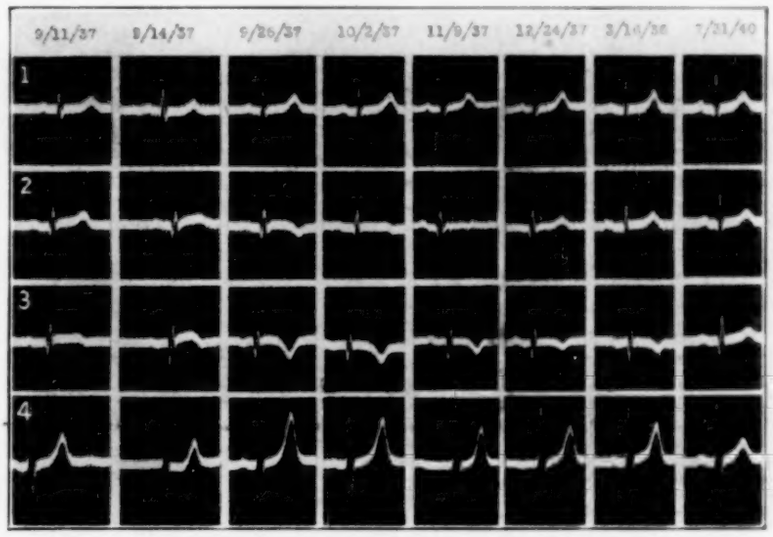

Fig. 3.—Serial electrocardiograms of a man aged 38 who sustained an acute coronary occlusion, Sept. 10, 1937. The deep Q_2 and Q_3, elevated RS-T in leads 2 and 3 and depressed RS-T in lead 4, progressing to inverted T_2 and T_3 and tall T_4, are characteristic of posterior wall infarction. The T waves gradually returned to normal. Three years after the attack the record is normal except for a persistent Q_3. Clinical recovery was good; the functional tests became normal. Activities were only slightly restricted and the patient returned to light work.

ELECTROCARDIOGRAM AFTER STANDARD EXERCISE

In recent years changes in the electrocardiogram following exercise have been studied in patients with chronic coronary disease.[27] Alterations may be produced similar to those observed during spontaneous attacks of angina pectoris, following anoxemia and in coronary insufficiency. They consist of transitory depression of the RS-T segment with or without lowering or inversion of the T waves. The test is often of great diagnostic value, particularly when the control electrocardiogram is normal or shows only minimal changes. We[9] have modified the test by using the two step exercise and by standardizing the amount of exercise performed on the basis of the same sex, age and weight tables used in the two step exercise tolerance test previously described.[28] In fact, the two tests, the ordinary exercise tolerance test and the electrocardiogram after exercise, can be performed simultaneously.[28] A positive result consists in the depression of the RS-T segment of more than 0.5 mm. below the PR interval or the flattening or the inversion of the T wave in one or more leads or a combination of these findings (fig. 4).

Electrocardiograms following standard exercise were obtained of 57 patients (table 6). For purpose of analysis they were divided into two groups, 18 whose electrocardiogram had returned to normal or almost normal and 39 whose electrocardiogram had remained abnormal. In the former group the test was positive in 5 (38 per cent), in the latter group in 24 (62 per cent). The test of 2 patients of each group was negative after standard exercise, but it became abnormal with double the standard amount of exercise.

In 1 of the 5 cases with normal control electrocardiograms and abnormal changes following standard exercise the test presented the only objective evidence of coronary insufficiency. All the other examinations in this case were negative despite the presence of a moderately severe anginal syndrome.

A negative electrocardiographic response to standard exercise was generally associated with a good clinical recovery, a normal test being obtained in three fifths of the good recovery group and in only one fifth of the poor recovery group (table 8). It must be remembered, however, that in the latter group the control electrocardiogram was usually abnormal.

Summarizing our electrocardiographic findings, it is apparent that return of the electrocardiogram to normal following coronary occlusion is associated with good cardiac function. This is borne out by the fact that of the 18 cases with a normal control electrocardiogram 13 showed a normal response in the electrocardiogram to exercise and in 12 the ordinary exercise tolerance

27. Riseman, J. E. F.; Waller, J. V., and Brown, M. G.: The Electrocardiogram During Attacks of Angina Pectoris: Its Characteristic and Diagnostic Significance, Am. Heart J. **19**: 683-707 (June) 1940. Feil, Harold: The Chest Lead Electrocardiogram in Chronic Cardiac Anoxemia, in Blood, Heart and Circulation; Symposium, Washington, D. C., American Association for the Advancement of Science, pp. 163-169.

28. Master, A. M.: The Electrocardiogram After Exercise: A Standardized Heart Function Test, U. S. Naval M. Bull. **40**: 346 (April) 1942.

(determined by pulse rate and blood pressure response) was also normal. On the other hand, the majority of the cases showing coronary insufficiency in the electrocardiogram after exercise had a reduced exercise tolerance (fig. 4).

RELATION OF FUNCTIONAL TESTS TO CLINICAL COURSE

We have already stressed the prognostic importance of the various objective tests utilized in this study. We have shown that the incidence of abnormal findings was distinctly greater among patients who made a poor or incomplete recovery than among those whose recovery was good (table 8). The converse of this observation also was true; that is, the probability of a good recovery was much greater for those patients whose objective tests remained or returned to normal. This applied particularly to the exercise tolerance test, ventricular pulsations and electrocardiogram. In fact, if one or more of these three examinations remain or return to normal following the acute attack recovery is good, with

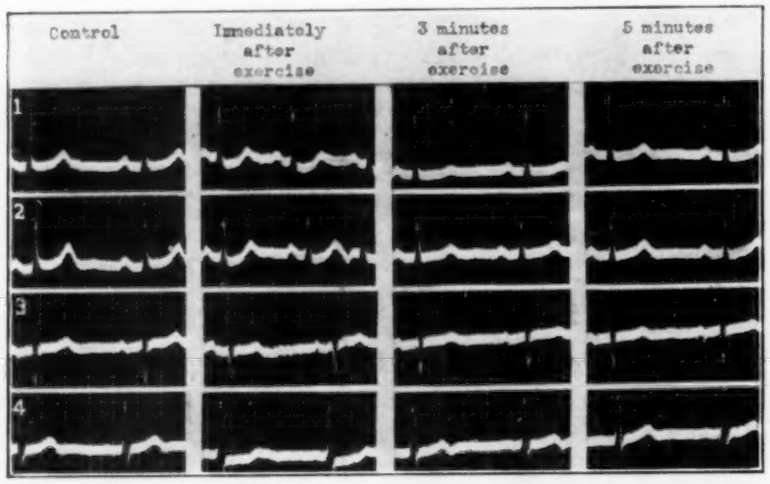

Fig. 4.—Electrocardiogram after the standard two step exercise tolerance test in a man aged 57 who sustained an acute coronary occlusion with anterior infarction seven years before. Control is normal except for left axis deviation. Immediately after twenty-one climbs the RS-T segment becomes depressed in leads 1, 2 and 4. Three minutes after exercise T_1 is low and T_4 diphasic. The record returns to normal within five minutes. These changes indicate transient coronary insufficiency induced by exercise. Although the electrocardiogram had returned to normal following the occlusion, the patient suffered from moderate angina pectoris and was unable to work. Exercise tolerance and ventricular pulsations remained abnormal. The patient died suddenly following another coronary occlusion four months after this test.

very rare exceptions. The same general rule can be applied to the electrocardiogram after standard exercise, but the number of exceptions is slightly greater. It is not true of the vital capacity and heart size for, as we have shown, these may be normal despite a poor clinical recovery. Nevertheless, the frequency of a normal vital capacity or cardiac size fell proportionately with the degree of disability of the patient. In a general way it may be stated that among the patients whose recovery was poor and whose functional capacity was much restricted the heart was enlarged, localized systolic expansion of the left ventricular contour was observed fluoroscopically, the electrocardiographic pattern of previous infarction persisted, the exercise tolerance test was distinctly below normal and the vital capacity was reduced, particularly if left heart failure was present.

TABLE 6.—*Electrocardiogram After Standard Two Step Exercise*

A. Normal control electrocardiogram		18
Normal response	13 (72%)	
Abnormal response	5 (28%)	
B. Abnormal control electrocardiogram		39
Normal response	15 (38%)	
Abnormal response	24 (62%)	

The relation of the functional tests to clinical recovery was studied also by correlating the results of these tests with the presence or absence of angina pectoris and dyspnea, the two most common causes of disability following recovery from coronary occlusion. The results are presented in table 9. It is seen that in the group of patients who had no significant angina or dyspnea there was a lower incidence of abnormal tests.

Of special interest is a group of 6 patients, in whom all the objective tests actually became normal. The findings in this small group emphasize the point that an attack of acute coronary occlusion, if not very severe, may be followed by complete functional and anatomic recovery, as far as can be clinically determined (fig. 2). In the remaining 60 patients who made a good clinical recovery at least one of the tests remained abnormal, although the patients returned to normal activity and were able to work.

RELATION OF FUNCTIONAL TESTS TO FUTURE ATTACKS

The results of the tests differed widely in the patients who subsequently sustained another attack of acute coronary occlusion or developed acute congestive heart failure from those in whom another attack did not occur (table 10). The results of each test were abnormal more frequently in the former group. In fact, in those who had another attack the ventricular pulsations and electrocardiogram were almost universally abnormal and an enlarged heart and diminished exercise tolerance were present in the great majority. In the presence of a normal electrocardiogram or ventricular pulsation a subsequent attack of either coronary occlusion or heart failure or subsequent death was exceedingly rare.

SUMMARY

1. Cardiac efficiency was studied by various function tests performed serially on 202 patients, who were observed for two to eight years following recovery from acute coronary occlusion. The results were evaluated from a prognostic point of view.

2. Recovery from acute coronary occlusion was found to be good or complete in over one third of the patients; i. e., they had no symptoms of diminished cardiac reserve or routine activity. One half were able to return to work, usually full time, and cardiac reserve, as measured by function tests, was normal or only slightly abnormal.

3. A persistent reduction in vital capacity was rare in the good recovery group but common in those whose recovery was poor. However, the vital capacity not infrequently was normal in the presence of severe angina pectoris. A reduction below 2,000 cc. was generally found only among patients who were in congestive heart failure.

4. The two step exercise tolerance test, a simple nonstrenuous test of cardiac function, became normal in 18 per cent and remained distinctly abnormal in two thirds of the patients. Return to normal usually

occurred one or two years after the attack and was associated with a good clinical recovery and decreased incidence of subsequent attacks.

5. The teleoroentgenogram revealed definite cardiac enlargement in half of the patients, and the majority of these were hypertensive. As a general rule chronic coronary sclerosis or coronary occlusion did not produce cardiac enlargement unless hypertension or heart failure was present. Although a severe degree of coronary disease may exist without cardiac enlargement, clinical recovery was more complete and subsequent attacks were less common when the heart size was normal, emphasizing the relation between heart size and cardiac function. Cardiac enlargement was always permanent.

6. A systolic expansion of the left ventricle, pathognomonic of previous infarction, was observed fluoroscopically or roentgenkymographically in nearly three fifths of the patients, and localized absence or diminution of pulsation in 25 per cent. With few exceptions these abnormalities were permanent. Although an abnormal ventricular pulsation did not preclude a good recovery from the attack, it was almost universal in those whose recovery was poor. Not infrequently it was the only remaining sign of previous infarction, being observed in the majority of patients whose electrocardiogram returned to normal. The patients with normal pulsations usually recovered completely and rarely sustained another attack.

7. The electrocardiogram returned to normal or almost normal in 21 per cent of the patients, usually within one year after the attack. The great majority of these made a good recovery, as well as those whose T waves became normal although the Q waves persisted. However, the persistence of the findings characteristic of previous infarction, which was observed in almost two thirds of the patients, was not necessarily a bad prognostic sign. The location of the infarct, i. e. whether anterior or posterior, did not affect the clinical course. However, when infarction of both surfaces had occurred the prognosis was worse.

TABLE 7.—*Time of Return to Normal* of Functional Tests*

	Vital Capacity	Exercise Tolerance	Ventricular Pulsations	Electrocardiogram
1 month	25	..	2	6
2-5 months	29	11	4	5
6-11 months	14	2	4	5
1 year	18	20	2	11
2 years	8	13	4	5
3 years	5	7	3	7
4 years	0	4	0	3
	99	57	19	43

* Normal or slightly abnormal.

TABLE 8.—*Positive Functional Tests and Clinical Recovery*

	Recovery			
	Good	Fair	Poor	Total
Number of cases	66	57	79	202
Vital capacity	12%	25%	62%	34%
Exercise tolerance	42%	60%	86%	65%
Heart size	32%	51%	68%	51%
Ventricular pulsations	70%	87%	94%	83%
Electrocardiogram	65%	68%	97%	79%
Electrocardiogram after exercise	39%	64%	80%	51%

Percentages indicate abnormal results.

8. The electrocardiogram after the standard two step exercise revealed signs of coronary insufficiency (depression of RS-T or inversion of T wave) in 5 of 18 patients whose control record was normal and in 24 of 39 patients with abnormal electrocardiograms. A negative test was associated with a good recovery and good cardiac function.

TABLE 9.—*Positive Functional Tests and Angina Pectoris and Dyspnea*

	No Angina Pectoris or Dyspnea	Angina Pectoris or Dyspnea
Number of cases	60	142
Vital capacity	9%	40%
Exercise tolerance	48%	79%
Heart size	38%	57%
Ventricular pulsations	60%	90%
Electrocardiogram	73%	82%
Electrocardiogram after exercise	31%	67%

Percentages indicate abnormal results.

TABLE 10.—*Positive Functional Tests and Further Attacks of Coronary Occlusion or Heart Failure*

	No Further Attacks	Subsequent Coronary Occlusion	Subsequent Heart Failure	Subsequent Deaths
Number of cases	137	46	17	34
Vital capacity	24%	45%	82%	63%
Exercise tolerance	55%	70%	100%	83%
Heart size	39%	70%	88%	88%
Ventricular pulsations	79%	93%	100%	97%
Electrocardiogram	72%	91%	100%	97%

Percentages indicate abnormal results.

9. The presence of a normal two step exercise tolerance test, normal ventricular pulsation or a normal electrocardiogram following coronary occlusion was usually accompanied by complete clinical recovery. Not only were significant angina pectoris and dyspnea uncommon when the foregoing tests became normal but a subsequent attack of either coronary occlusion or heart failure was rare. In those whose recovery was poor there was nearly always objective evidence of disability.

ABSTRACT OF DISCUSSION

DR. CARY EGGLESTON, New York: On the basis of clinical experience and a recognition of the essential nature of the damage usually caused in myocardial infarction, one would be inclined to suspect a priori that no single objective test could be expected to yield results of significant value in prognosis as to degree of recovery of cardiac function. This a priori judgment appears to be confirmed by the results recorded in the paper of Drs. Master, Dack and Jaffe, although this does not impair the great value inherent in their study. Their results show that, on clinical judgment alone and without the application of any test, one third of the patients made a good recovery, 40 per cent a poor recovery and nearly 30 per cent a recovery intermediate between these two. When an effort was made to utilize one of the simplest of all measures of cardiac function, namely the vital capacity, the results obtained scarcely justified the time spent, except in the small group of cases in which infarction is followed by congestive failure. This result, I think, was to have been anticipated, since lasting disability following infarction generally rests on the persistence of the development of angina pectoris as the limiting factor to the patient's activities. The second test applied, that of exercise tolerance, similarly gave results in fairly close conformity to those which were to be expected; that is, it confirmed the experience just mentioned, that where there is subsequent limitation of cardiac function it is generally due to the development or the persistence of the manifestations of angina pectoris. The authors have recognized these facts. My comments are not intended in any way to minimize the importance of this study. My criticisms are made to point out what appears to be the

most important conclusion to be drawn from this study; namely, that while several tests may be employed for judgment of the degree of recovery of cardiac functional integrity after infarction, the results of such tests scarcely yield enough, when compared to clinical experience and good clinical judgment, to make the expenditure of time and labor worth while. I feel skeptical about the ability of any tests, alone or in combination, to provide a trustworthy foundation for prediction as to the probability of the patient's suffering a subsequent infarction. I remain to be convinced that that is true in a large series of cases—and 200 is not very large in a condition so common and diverse in its course as myocardial infarction. There is a field in which these tests may have much application; namely, in the solution of medicolegal problems based on the determination of the degree of restoration of heart function, for they certainly are capable of yielding objective data which can well be of more or less determinative value to present to a court.

DR. HOWARD B. SPRAGUE, Newport, R. I.: The fact stated that 40 per cent of patients who suffer from myocardial infarction return to fairly active lives is very encouraging. It shows how far we have come from the time when the diagnosis of coronary occlusion was considered essentially an immediate death sentence. It was stated that about half of the patients had cardiac enlargement and that about half had abnormal ventricular pulsations. I should like to know whether this half of the patients who had the big hearts were the half who had the abnormal ventricular pulsations. When I see cardiac enlargement following myocardial infarction under the fluoroscope I am influenced to discover that there are abnormal ventricular pulsations and do not so frequently see such a beautiful demonstration of reversal of pulsations as was shown on the screen. As far as the electrocardiogram is concerned, I agree; as has been shown before, the failure of the electrocardiogram to return to normal does not mean that the patients will have a poor prognosis. I have the feeling that the rapidity with which the electrocardiogram during the acute stage defines itself as of the anterior-posterior type and the speed at which the ST displacements return to normal are the important immediate prognostic elements. The point is important that the patient will largely have recovered as much as he will in a year as far as all these objective tests are concerned. That is my clinical opinion. Perhaps the best and the simplest way to discover whether or not a patient has made a recovery from myocardial infarction is first to find out how big his heart is and, second, whether he has shortness of breath or signs of angina pectoris when he gets about.

DR. ARTHUR M. MASTER, Bethesda, Md.: There is always a disinclination to learn new methods or new tests and that is the situation in Dr. Eggleston's case. In a long experience in clinical practice and in research we have found functional tests valuable and have used them constantly. The military forces too have found them indispensable. To learn the value of function tests one necessarily assays them on patients who are in an obviously poor or good clinical condition. Once the value of the tests is thus proved they are performed on patients in whom the diagnosis or prognosis is in question. The tests are as useful in a prognostic sense as in a diagnostic. The tests described are simple and are objective for the most part. This makes them particularly valuable since one does not always obtain the whole truth from the patient. He may be hyposensitive or his history may be colored by insurance or compensation angles. With regard to enlargement of the heart and the ventricular pulsations, one does see a higher incidence of systolic expansions or reversals on fluoroscopy in large hearts. We have published our figures. However, one will just as definitely see the systolic expansion in small hearts and often more clearly since there is more lung background. As a matter of fact my very first observation occurred in 1933 on a woman with a very small heart. As to the facilities for observing these abnormal cardiac pulsations on the fluoroscope, one should have a good Patterson B screen. However, it is preferable, but not necessary, to have some one actually demonstrate the fluoroscopic changes we have described. It is good to possess a healthy skepticism but we overcame this four or five years ago. We proved our case by actual demonstration. Patients were sent into the dark room and we were asked to pick out those with systolic expansions, i. e. patients who had had coronary occlusion previously. We were able to do it. I might add that after a little training my pharmacist and corpsmen at the National Naval Medical Center in Bethesda make the fluoroscopic diagnosis of coronary occlusion without difficulty.

CHRONIC MOUNTAIN SICKNESS

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LIMA, PERU

The resident of high altitudes, native or newcomer, lives in a condition of chronic anoxia, as shown by the lowering of the arterial oxygen saturation.[1] The existence of a complete adaptation to this condition, when moderate or severe in degree, and the level of altitude at which the required compensatory processes cease to be within physiologic limits still remain as problems to be elucidated.

In 1928 Monge [2] indicated that an accentuation of the polycythemia commonly found in residents of high altitudes constitutes a main alteration among the various conditions which characterize the loss of tolerance to a low barometric pressure environment. In subsequent writings Monge [3] described the symptoms and signs which accompany the hematologic disorder to which the names of chronic mountain sickness, high altitude erythremia and Monge's disease have been given. The disappearance of the polycythemia on descent to a lower altitude or to sea level is, according to Monge, a basic aspect of the condition.

The present communication concerns observations made in 8 of these cases in an effort to obtain some information regarding the underlying etiologic mechanism or mechanisms. The patients were men of Indian race, born and living at altitudes between 4,000 and 4,500 meters (13,120 to 14,760 feet) and of an age ranging between 24 and 44 years. Six of the men were studied at high altitudes and two of them immediately after arrival at sea level. None of them had previously worked in mines or foundries or in any other dusty occupation.[4] Among their most common symptoms may be cited headache, dizziness, ringing in the ears, vague pain in the extremities, cough, shortness of breath on exertion, palpitation, moderate hemoptysis, epistaxis and gastric distress with a feeling of indigestion. Cyanosis, dilated superficial vessels and a moderate to a conspicuous clubbing of the fingers and toes were

From the Department of Pathologic Physiology, Faculty of Medicine and the National Institute of Andean Biology.

Read before the Section on Pathology and Physiology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

1. Barcroft, J.; Binger, C. H. L.; Bock, A. V.; Doggart, J. H.; Forbes, H. S.; Harrop, G.; Meakins, J. C., and Redfield, A. C.: Tr. Roy. Soc. **211**: 351, 1922. Monge, Carlos; Heraud, C.; Encinas, E., and Hurtado, A.: Estudios Fisiológicos sobre el hombre de los Andes, Facultad de Medicina, Lima, 1928. Hurtado, Alberto: Am. J. Physiol. **100**: 487, 1932. Stammers, A. D.: J. Physiol. (Proceedings of the Physiological Society) **78**: 21P, 1933. Talbott, J. H., and Dill, D. B.: Am. J. M. Sc. **192**: 626, 1936.

2. Monge, Carlos: La Enfermedad de los Andes (Sindromes Eritrémicos), An. Facultad de Medicina, Lima, 1928.

3. Monge, Carlos: High Altitude Disease, Arch. Int. Med. **59**: 32 (Jan). 1937; Life in the Andes and Chronic Mountain Sickness, Science **95**: 79 (Jan. 23) 1942; Les érythrémies de l'altitude.[7] La Enfermedad de los Andes.[7]

4. The hematologic and other alterations found in cases of pneumonoconiosis (silicosis), which have been interpreted as being due in part to an associated chronic mountain sickness (Monge: Life in the Andes and Chronic Mountain Sickness[3]) are, in my opinion, solely related to the increased arterial unsaturation caused by the pulmonary changes present in the former disease and are similar in nature to those observed at sea level in cases which show some degree of anoxemia. The improvement or disappearance of the symptoms on descent to a lower altitude is a consequence of the higher arterial saturation under these circumstances. Oxygen at the normal partial pressure of sea level may be able to diffuse better through a thick alveolar membrane, less permeable when the gas is at reduced tension at high altitudes.

prominent features in all of them. Liver, spleen and glands were not palpable. The blood Kahn reaction was positive in case 5. The physical characteristics corresponded to their Indian race (average height 1.57 meters, average weight 55.4 Kg.); the nutritional condition was normal in every case.

The results obtained in the various hematologic observations are given in tables 1 and 3 and are partly presented, graphically, in figure 1.

In another communication [5] the hematologic characteristics observed in healthy native residents at different altitudes were discussed. The comparison of those results with the ones found in these cases reveals a considerable rise in the red blood cells, hemoglobin, hematocrit reading, viscosity and bilirubin in the men showing signs and symptoms of chronic mountain sickness. In 2 cases the circulating reticulocytes were

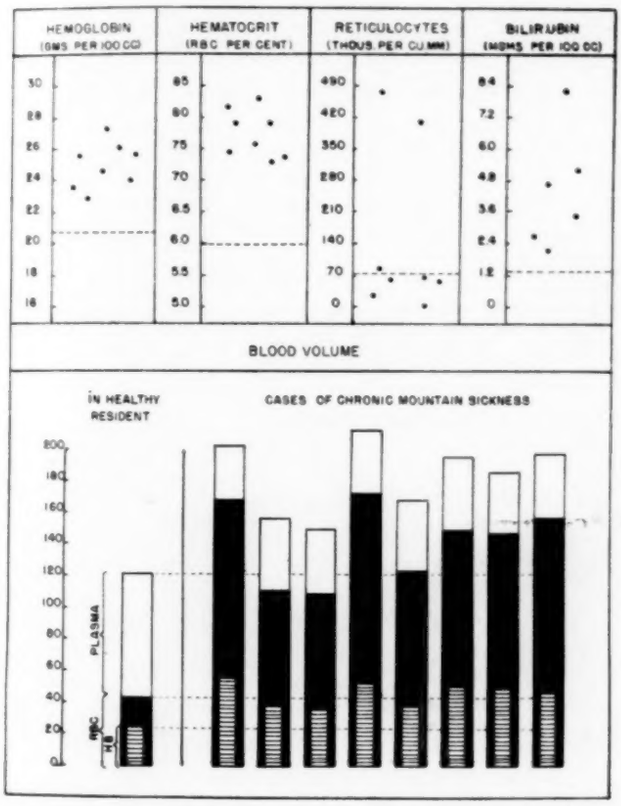

Fig. 1.—Hematologic observations in 8 cases of chronic mountain sickness (at an altitude of about 4,450 meters, 14,900 feet). Findings compared with mean values observed in healthy residents at that altitude (upper horizontal interrupted lines).

abnormally elevated. No significant changes were observed in the morphologic characteristics of the circulating red cells with the exception of a moderate lowering of the corpuscular hemoglobin concentration in 3 cases. The blood volume determinations showed a decided increase in the circulating red cell volume and hemoglobin and a decrease in the plasma volume. The total blood volume was elevated. These findings correspond to an absolute polycythemia of the type of polycythemic hypervolemia, in agreement with the original observation [6] made in 1937. The leukocytic concentration and differential count were similar to those found in healthy residents.

5. Hurtado Alberto: The Influence of Anoxemia on the Hemopoietic Activity, read in the General Scientific Meetings at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 8, 1942.

6. Hurtado A.: Aspectos Fisiológicos y Patológicos de la Vida en la Altura, Editorial Rimac., Lima, 1937.

Figures 2 and 3 correspond to the blood volume determinations made on some of the subjects after they had been taken down to sea level. It may be observed that in all cases, with the exception of 1 observed thirty days after arrival, a considerable decrease occurred in the circulating blood volume brought about by the low-

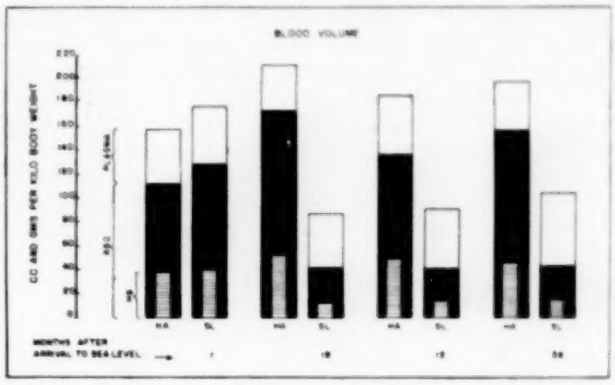

Fig. 2.—Circulating blood volume and hemoglobin (expressed in cubic centimeters and grams per kilogram of body weight) in cases of chronic mountain sickness studied at high altitudes (*HA*) and after descent to sea level (*SL*).

ering of the red cell volume. There was a moderate increase in the plasma volume. The series of determinations made in case 5 (fig. 3) have an interesting aspect on account of the prolonged time the man was under observation, both at high altitudes and at sea level. A rise in the plasma volume paralleled the decrease in the cell volume when this subject was living at sea level. I have observed this phenomenon in some other cases (unpublished observations) during the first weeks of residence at sea level.

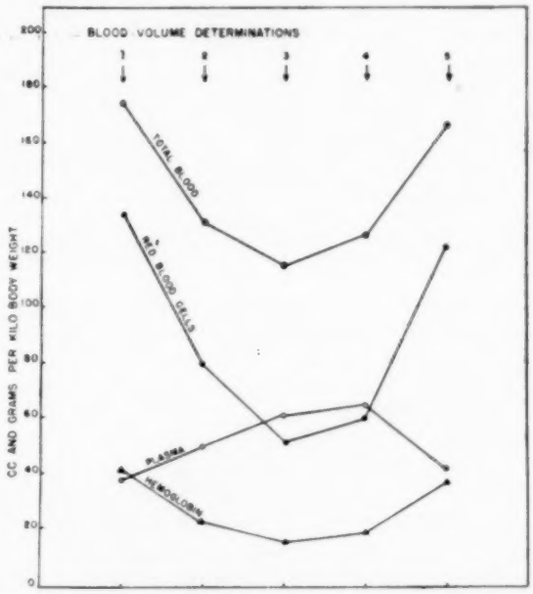

Fig. 3.—Circulating blood volume and hemoglobin (expressed in cubic centimeters and grams per kilogram of body weight) in case 5 of chronic mountain sickness: first determination twelve days after arrival from high altitudes; second determination sixty-four days after arrival; third determination one hundred and three days after arrival; fourth determination nine days after having spent a week at high altitudes; fifth determination made at high altitudes after eleven months of residence.

The disappearance of the polycythemia at sea level was accompanied in all cases by the cessation of the symptoms enumerated.

It is not known at the present time which is the factor or factors responsible for the abnormal accentua-

tion of the polycythemia which exists in some degree in all residents of high altitudes. Monge in his publications, already cited, has stressed the apparent similarity of the hematologic alterations found in these cases of chronic mountain sickness with those observed in polycythemia vera, and in his early papers,[7] referring to the studies of Harrop and Heath [8] in the latter disease, explained the accentuation of the high altitude polycythemia on the basis of a decreased alveolar permeability for the passage of oxygen. In another communication [5] it was shown that the level of the absolute polycythemia found in residents of high altitudes has a striking direct correlation with the degree of the arterial oxygen unsaturation, suggesting that the latter factor constitutes the fundamental stimulus for the erythropoietic hyperactivity. In the presence of an abnormally high level of polycythemia, such as has been found in our cases, three etiologic possibilities may be considered: It may be due, in the first place, to a heightened rate of erythropoietic activity independent of any known stimulus, a condition somewhat analogous to what occurs in polycythemia vera, or to a more active response on the part of the bone marrow to the anoxic stimulus which corresponds, in a normal degree, to the altitude at which the man lives; or, and this is the third possibility, the more accentuated polycythemia is the consequence of a more pronounced arterial unsaturation brought about by pulmonary, circulatory or other abnormalities.

With regard to the first possibility, I do not believe that there is any similarity between the normal or accentuated polycythemia of high altitudes and the one corresponding to polycythemia vera, beyond the increase in the red cell volume which is found in all these processes. All investigators agree on the fact that in polycythemia vera there occurs very frequently an increase in the white blood cells with evidence of a pathologic leukoblastic activity as shown by the presence of immature cells in the peripheral blood. Such compromise of the leukocytic series is never found at high altitudes [5] no matter how elevated is the level of polycythemia, and the same thing is true in the cases I am discussing. This fact, among others, is a most serious objection to the acceptance of the view that anoxia of one type or another is responsible for the development of polycythemia vera, which seems to be more adequately explained, as it has been suggested, by a disorderly activity of the entire hemopoietic system.

The abnormal accentuation of the polycythemia may be related to an exaggerated response of the erythropoietic organs to the arterial oxygen unsaturation which exists at high altitudes and which depends on the low partial pressure of oxygen in the atmosphere. However, the fact that the arterial oxygen saturation in all but 1 of the cases is lower than what corresponds to the given altitude (fig. 4) suggests that the high level of polycythemia is a consequence of the increased anoxic stimulus, an assumption which has some support on the observations [5] made in nearly 100 cases of silicosis developed in mines located in elevated places, in which the more pronounced arterial oxygen unsaturation, brought about by the pulmonary changes, was accompanied by a higher level of polycythemia. Incidentally it may be mentioned that the arterial oxygen saturation has been found to be unchanged in cases of polycythemia vera,[9] a further point of differentiation between the two conditions.

There remains to be considered the possible mechanism responsible for the abnormal degree of anoxemia in these cases. We cannot rule out the possibility that this is a secondary effect, rather than a causal factor, to the increased pulmonary vascularity resulting from

TABLE 1.—*Hematologic Observations in Cases of Chronic Mountain Sickness*

Cases	Red Blood Cells (Millions per Cu. Mm.)	Hemoglobin (Gm. per 100 Cc.)	Hematocrit (RBC per Cent)	Corpuscular Volume (Cu. Micrograms)	Corpuscular Hemoglobin (Micro-micrograms)	Corpuscular Hemoglobin Concentration (per Cent)	Reticulocytes (per Cent)	Bilirubin (Mg. per 100 Cc.)	Leukocytes (per Cu. Mm.)	Viscosity
1	9.35	27.17	83.0	88.7	29.1	32.8	4.4	8.33	3,800	28.8
2	7.37	25.57	74.6	101.2	34.6	34.2	1.2	2.24	6,400	15.6
3	8.63	24.01	73.0	84.6	27.8	32.8	0.6	5.55	6,210	14.6
4	8.50	24.60	81.7	96.1	28.9	30.1	5.6	2.67	7,200	23.4
5	7.70	22.89	73.7	95.7	29.8	31.1	0.8	3.52	6,800	....
6	7.61	25.78	75.7	99.5	33.8	34.0	0.8	....	5,800	....
7	8.00	26.13	79.2	99.0	32.7	33.0	0.3	4.59	6,100	....
8	8.97	23.50	79.2	88.3	26.2	29.7	0	....	6,400	....

The hemoglobin was calculated from the oxygen combining capacity determined in the Van Slyke manometric apparatus (Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, vol. 2, Methods, Baltimore, Williams & Wilkins Company, 1932); for the hematocrit a Wintrobe tube centrifuged for forty-five minutes at 3,000 revolutions per minute was used; the bilirubin was determined with a colorimetric procedure (Guzmán Barrón, S.: Medicine **10**: 77, 1931) and for viscosity a Hess viscosimeter was employed.

TABLE 2.—*Respiratory Investigations in Cases of Chronic Mountain Sickness*

	Place of Study, Altitude		Arterial Blood				Pulmonary Capacity		
Cases	Meters	Feet	CO_2 Content (Vol. %)	HbO_2 Content (Vol. %)	HbO_2 Capacity (Vol. %)	HbO_2 Saturation (per Cent)	Residual Air (Liters)	Vital Capacity (Liters)	Total Capacity (Liters)
1	3,730	12,240	34.59	28.20	36.42	77.4	1.28	2.75	4.03
2	3,730	12,240	33.41	28.45	34.28	82.9	2.22	3.63	5.85
3	3,730	12,240	35.11	24.53	32.29	75.9	2.49	2.24	4.73
4	3,730	12,240	32.13	26.17	32.97	79.4	1.82	3.15	4.97
5	4,540	14,900	35.70	23.44	30.81	76.1	1.92	4.46	6.38
6	4,540	14,900	29.00	26.66	34.49	77.3	2.55	3.32	5.87
7	Sea level		38.97	33.59	35.03	95.9	....	....	....
8	Sea level		36.36	29.98	32.85	91.2	1.27	2.84	4.11

The gas analysis of the arterial blood, obtained under anaerobic conditions from the radial artery, was made in the Van Slyke manometric apparatus; the pulmonary capacity was determined according to Christie's method (Quart. J. Med. **11**: 1099, 1932) in the sitting position.

7. Monge, Carlos.: Les érythrémies de l'altitude, Paris, Masson et Cie, 1929; La Enfermedad de los Andes (Sindromes Eritrémicos), Rev. Med. Per. Lima **2**: 7, 1929; La Enfermedad de los Andes.[3]

8. Harrop, G. A., and Heath, E. H.: J. Clin. Investigation **4**: 53, 1927.

9. Altschule, M. D.; Volk, M. C., and Henstell, H.: Am. J. M. Sc. **200**: 478, 1940.

the elevated circulating blood volume. Against this possibility is the observation [9] that in polycythemia vera the arterial oxygen saturation is normal in spite of the tremendous increase in the cell volume, and the investigations of Dill, Christensen and Guzmán Barrón,[10] who have pointed out that in residents of high altitudes, even at the highest places with the corresponding polycythemia, the partial pressure of oxygen in the alveolar air plays the major role in the acquisition of this gas by the circulating hemoglobin. If the blood circulating normally in the lung capillaries acquires less oxygen than what corresponds to the tension of this gas in the alveolar spaces, the causative mechanism, ruling out changes in the hemoglobin affinity for oxygen, may be related to either one, or both, of the following alterations: (*a*) a deficient ventilation of the alveoli and (*b*) a decreased permeability of the alveolar membrane for the passage of oxygen. Condition *a* is brought about mainly by shallow breathing, a respiratory irregularity not found in the cases now under discussion and by a process of emphysema in which the loss of elasticity and the abnormal distention of the alveoli make difficult the adequate removal and distribution of the air. Determination of the total lung volume and its subdivisions, made in 7 of the 8 cases studied (table 2), do not reveal the great increase in residual air which characterizes pulmonary emphysema; in addition, the vital capacity is only moderately reduced. It seems, therefore, that an emphysematous condition of the lungs is not responsible in these cases for the abnormal degree of anoxemia.

TABLE 3.—*Blood Volume Determinations in Cases of Chronic Mountain Sickness*

Cases	Blood (Cc. per Kg.)	Plasma (Cc. per Kg.)	Red Blood Cells (Cc. per Kg.)	Hemoglobin (Gm. per Kg.)
1	202.9	33.4	168.3	55.1
2	157.1	37.1	111.1	38.1
3	149.6	39.6	109.2	35.9
4	211.9	27.7	173.1	53.1
5	167.2	43.1	123.3	38.4
6	196.6	46.8	148.8	50.6
7	186.2	37.8	147.3	48.6
8	197.8	40.2	156.7	46.5

The blood volume was determined by the method of Keith, Rowntree and Geraghty (Arch. Int. Med. **16**: 547 [Oct.] 1915) with the modifications of Hooper, Smith, Belt and Whipple (Am. J. Physiol. **51**: 205, 1920). A 1.5 per cent solution of brilliant vital red was employed.

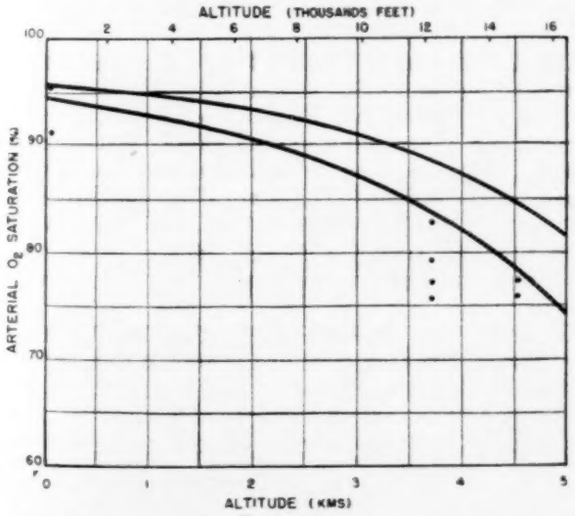

Fig. 4.—Arterial oxygen saturation in 8 cases of chronic mountain sickness, 2 cases studied at sea level; 4 cases observed at an altitude of 3,730 meters (12,240 feet) and 2 cases studied at an altitude of 4,540 meters (14,900 feet). Zone between heavy lines corresponds to the normal limits of variation of the arterial oxygen saturation at different altitudes.

As a final consideration, the possible existence of organic changes which would cause a decreased diffusion for oxygen may be briefly discussed. Roentgenograms (fig. 5) taken in 7 of the cases revealed a definite accentuation in the lung markings on both sides, persistent in 2 of them at sea level even after the disappearance of the polycythemia. In 5 cases the heart was abnormally large, as observed in the chest roentgenogram, and the electrocardiogram showed a right ventricular preponderance. In 2 the tracings were normal. In 2 cases there were clinical signs of cardiac insufficiency of the right type. The blood pressure was normal or moderately low.

These observations suggest the presence of fibrosclerotic changes in the lungs of these men, changes which may correspond to those observed in the ill defined group in which the so-called Ayerza syndrome is placed and which frequently originates a pronounced unsaturation of the arterial blood. Several factors would favor at high altitudes the development of these organic changes in the lungs. Anoxemia, per se, may be an important factor. Campbell [11] has observed a thickening of the pulmonary arterioles in animals subjected for several weeks to a low barometric pressure, and Büchner and Luft [12] have reported the occurrence of degenerative arterial lesions under similar experimental conditions. In 1930 I [13] found pulmonary sclerosis in a man, not a miner, living at an altitude of 4,500 meters (14,760 feet), but the value of this observation was limited by the absence of previous clinical data. The fibrous changes in the lungs developed after repeated pneumothorax may be due in great part to the lack of oxygen supply during the periods of collapse.

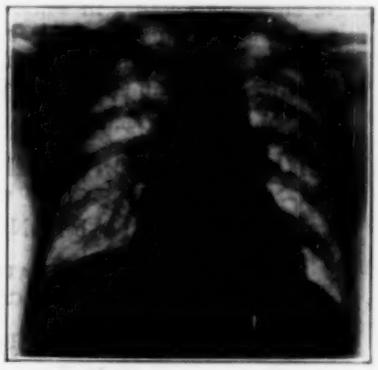

Fig. 5.—Appearance of the chest in case 6.

An increased tension in the pulmonary vascular bed has been found clinically [14] and experimentally [15] to cause arteriosclerosis. It seems that this portion of the vascular system is especially susceptible to variations in pressure. No direct measurement of the pulmonary arterial pressure has been made at high altitudes, but its possible elevation may be inferred from the permanent congestive condition and the greater volume of blood contained in the lungs [6] and from the high frequency of right ventricular preponderance in the electrocardiograms taken in apparently healthy natives.[16] The frequent respiratory infections and the

10. Dill, D. B.; Christensen, F. H., and Guzmán Barrón, E.: Am. J. Physiol. **115**: 530, 1936.

11. Campbell, J. A.: Brit. J. Exper. Med. **16**: 39, 1935.
12. Büchner, F., and Luft, V. C.: Beitr. z. path. anat. **46**: 54, 1936.
13. Hurtado, Alberto: Rev. méd. peruana, Lima, **1**: 1, 1930.
14. Miller, H. R.: M. Clin. North America **9**: 673, 1925. Ljundahl, M.: Untersuchungen über die Arteriosklerose des kleinen Kreislaufs, Wiesbaden, J. F. Bergman, 1915. Moschcowitz, Eli: Am. J. M. Sc. **174**: 388 (Sept.) 1927. Brenner, Oscar: Pathology of the Vessels of the Pulmonary Circulation, Arch. Int. Med. **56**: 211 (Aug.), 457 (Sept.), 724 (Oct.), 976 (Nov.), 1189 (Dec.) 1935. Parker, Frederic, Jr., and Weiss, Soma: Am. J. Path. **12**: 573 (Sept.) 1936.
15. Bennett, G. A., and Smith, J. C. F.: J. Exper. Med. **59**: 181, 1934.
16. Capdehourat, E. L.: Estudios sobre la Biología del hombre de la Altitud, Buenos Aires, 1937.

high viscosity of the blood may constitute additional factors in the tendency to develop anatomic alterations in the lungs at high altitudes.

The disappearance of the anoxemia and of the resulting polycythemia on descent to sea level is not a basic argument against the possibility that organic changes of the nature described are responsible for the increased arterial unsaturation found at high altitudes in some cases of chronic mountain sickness. It must be considered that the passage of oxygen through the alveolar membrane corresponds to a physical process of diffusion and that a thick membrane may constitute an obstacle for an oxygen with a partial pressure of about 50 mm. of mercury (41.5, 53.4 and 47.2 in cases 1, 2 and 4, respectively, studied at high altitudes) in the alveolar spaces, but it may allow a normal passage when such tension is raised at sea level on account of the higher barometric pressure.

The study of a greater number of cases and the anatomic investigation of the lungs and other organs after death will be necessary for the final understanding of the etiologic mechanism responsible for the hematologic alterations found in some cases of chronic mountain sickness. In this field, as in many others, the morphologic aspects have been unduly neglected in favor of the functional and chemical approximation.

OCHRONOSIS OF THE SCLERA AND CORNEA COMPLICATING ALKAPTONURIA

REVIEW OF THE LITERATURE AND REPORT OF FOUR CASES

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NEW YORK

Medical works of the sixteenth and seventeenth centuries cite instances of urines which were black when voided or which darkened on exposure to air. In 1858 Boedeker [1] found in the urine of a patient with glycosuria a second reducing substance, not a sugar, to which, on account of its behavior toward alkalis, he assigned the name alkapton. Marshall [2] in 1887 discovered the true nature of alkapton to be glycosuric acid. Wolkow and Bauman named the reducing substance homogentisic acid because it is a homologue of gentisic acid and showed that the peculiar properties of so-called alkaptonuric urine is due to this acid. Garrod [3] considers alkaptonuria as an inborn error of metabolism which is present at birth. When first voided, the urine of an alkaptonuric person appears of normal color but after contact with air undergoes a change through various shades of brown to actual blackness. The addition of an alkali will accelerate the color change. Linens and woolens moistened with the urine are stained as if by a photographic developer.

Alkaptonuric patients cannot effect the complete catabolism of the tyrosine and phenylalanine contained in the proteins of the food and tissues, so that an intermediate product, homogentisic acid (hydroquinoneacetic acid), remains. Homogentisic acid shares with other similar aromatic compounds the property of blackening on oxidation, which explains the characteristic property of alkapton urine. At least 200 cases of alkaptonuria have been reported. The disorder shows a family tendency, particularly in children of consanguineous parents, and is inherited as a recessive mendelian characteristic.

Virchow [4] in 1866 observed discoloration of cartilage during a postmortem examination. Under the microscope the pigment granules appeared pale yellow or ochre. He named the disease ochronosis. This observation passed unnoticed until a second case was reported twenty-five years later. In 1902 Albrecht [5] first suggested that alkaptonuria was the cause of ochronosis. Osler [6] in 1904 described the clinical features of the disease—pigmentation of the sclera, ear cartilage and a peculiar stance and gait. In 1906 Pick [7] reported a case due to prolonged use of phenol dressings to leg ulcers, which he described as exogenous ochronosis in contrast to the endogenous form of congenital origin associated with alkaptonuria.

The most plausible explanation of the mode of production of the pigment in the disease is by Pick. He suggested that, through the action of the oxidative ferment tyrosinase, the phenol substances in the exogenous group and the homogentisic acid molecule in the endogenous group are changed into melanin pigment, which is deposited in the tissues. Abderhalden and Guggenheim [8] believe that an accumulation in the human organism of excessive and abnormal amounts of substances possessing the oxyphenyl group leads to the production of melanin pigments by ferment action. Both the exogenous and the endogenous group contain this chemical entity. Clemens,[9] Wagner [10] and Landois [11] demonstrated the presence of pigmentation in cartilages and other structures.

Allard and Gross [12] described the deforming arthritis of the larger joints in alkaptonuria. In the family, reported by Umber and Burger,[13] of 8 children of an alkaptonuric father and a normal mother 4 were alkaptonuric. The alkaptonuric children suffered severely from articular lesions. The 4 nonalkaptonuric children were entirely free from arthritis. Soderbergh [14] in 1915 emphasized the roentgen changes in the vertebral column and suggested the name osteitis deformans alkaptonuria.

Clinically, ochronosis is first recognized by a blue coloration of the ears, first of the concha and antihelix and later of the tragus and antitragus. The darkened cartilages of the ears feel abnormally firm. In many instances the first sign is gray coloration of the scleras

From the Hospital for Joint Diseases and the Welfare Hospital.
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This article is abbreviated in THE JOURNAL by the omission of a colored plate, five tables and reading matter. It appears in complete form in the Transactions of the Section and in the author's reprints.

1. Boedeker: Ueber das Alkapton, Ztschr. f. rat. Med. **7**: 130 (no. 1) 1859.
2. Marshall, J., cited by Hammarsten, O.; Hedin, S. G., and Mandel, J. A.: Physiological Chemistry, ed. 8, New York, John Wiley & Sons, 1914, p. 735.
3. Garrod, A. E. Inborn Errors of Metabolism, ed. 2, London, Frawde, Hodder and Stoughton, 1923, pp. 43-64.
4. Virchow, Rudolf: Ein Fall von allgemeiner Ochronose der Knorpel und knorpelähnlichen Teile, Virchows Arch. f. path. Anat. **37**: 212, 1866.
5. Albrecht, H.: Ueber Ochronose, Ztschr. f. Heilk. **23**: 366, 1902.
6. Osler, William: Ochronosis, the Pigmentation of Cartilages, Sclerotics and Skin in Alkaptonuria, Lancet **1**: 10 (Jan.) 1904.
7. Pick, L.: Ueber die ochronose, Berl. klin. Wchnschr. **43**: 478, 1906.
8. Abderhalden, E., and Guggenheim, M.: Versuche über die Wirkung der Tyrosinase aus Russala delica auf Tyrosin, tyrosinhaltige Polypeptide und einige andere Verbindungen unter verschiedene Bedingungen, Ztschr. f. physiol. Chem. **54**: 331, 1907.
9. Clemens: Diskussion zur Alkaptonurie, Verhandl. d. deutsch. Kong. f. inn. Med. **24**: 249, 1907.
10. Wagner, A.: Ueber Ochronose, Ztschr. f. klin. Med. **65**: 119, 1908.
11. Landois, F.: Zur Kenntnis der Ochronose, Virchows Arch. f. path. Anat. **193**: 275, 1908.
12. Allard, E., and Gross, O.: Alkaptonurie und Ochronose, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **19**: 24, 1908-1909.
13. Umber and Burger: Alkaptonurie mit Ochronose und Osteoarthritis deformans, Zystinurie, Deutsche med. Wchnschr. **39**: 2337, 1913.
14. Soderbergh, G.: Zur Klinik der Alkaptonurie, insbesondere über die Wassermannsche Reaktion und Ostitis deformans alcaptonurica, Nord. med. Ark. **48**: part 2 (in re medicin) 19, 1915.

or brown pigment spots near the insertion of the rectus tendons. Areas where the blackened cartilages or tendons show through the overlying skin appear blue. Later, the nasal cartilages become stained, the nose may appear blue and a butterfly-shaped brown pigmentation of the skin of the face develops. Less frequently, the knuckles of the hands are blue owing to staining of the tendons, and in rare instances the thenar and hypothenar eminences are pigmented brown.

The postmortem examination reveals deep brown or raven black pigmentation of the cartilages, fibrocartilages, fibrous tissue and epidermis, as well as areas of degeneration, notably atherosclerotic plaques, albuminous masses and concretions.

GENERAL REVIEW OF THE LITERATURE

The importance of the scleral pigment spots has been stressed by internists since 1895, but ocular ochronosis has never been described in an American textbook on ophthalmology. I have reviewed every paper on ochronosis with particular reference to involvement of the eye.

Scant credit is given to American authors for their contribution to the clinical knowledge of alkaptonuria and ochronosis. Marshall in 1887 reported the first case of alkaptonuria in this country and discovered homogentisic acid. A case of alkaptonuria described by Ogden [15] in the *Zeitschrift für physiologische Chemie* in 1895 is revealed as having been presented before the Milwaukee Medical Society in 1890. Hecker and Wolf are universally credited as the first to describe the discoloration of the eyeball in 1899. Scleral pigmentation was first observed by Osler four years earlier. A historical note of ophthalmologic importance is that Osler's diagnosis of ochronosis in his first and second American patients was based on the eye changes which he described in minute detail. The second patient, whose condition was reported originally as alkaptonuria by Marshall, was a brother of the patient seen by Osler in 1895.

The third case of ochronosis was established by letter when Ogden wrote "the color of the inside of each concha is a pearly light grayish lead blue, like the inside of our common mussel shells."

Harvey Cushing's [16] finding that the first British case of ochronosis had been diagnosed as Addison's disease does not appear in the medical literature and is worth recording.

The most authoritative monograph on ochronosis is the one hundred and eighty-nine page doctorate thesis by Valdemar Poulsen [18] of Copenhagen in 1909. Every author outside of his country has quoted this reference as of German origin. No one ever sought to explain how a 30 year old investigator had the good fortune to observe 9 cases of such a rare disease. Through the courtesy of the New York Academy of Medicine, a copy of the thesis was obtained from the library of the Surgeon General's Office. Poulsen records the optic disorders present in 7 cases and 2 in which postmortem pathologic sections were made. Fifteen colored drawings depict in a graphic manner the outstanding clinical and pathologic manifestations in ochronosis.

15. Ogden, H. V.: Ein fall von Alkaptonurie, Ztschr. f. physiol. Chem. **20:** 280, 1895.
16. Cushing, Harvey: The Life of Sir William Osler, Oxford, Clarendon Press, 1925, vol. 1, p. 623; vol. 2, p. 11.
18. Poulsen, Valdemar: Om ochronotiske tilstande hos mennesker og dyr, Copenhagen, Jacob Lunds Medical Bookstore, 1910; Ueber ochronose bei menschen und tieren, translation, Beitr. z. path. Anat. u. z. allg. Path. **48:** 346, 437, 1910; Ueber einem neuen Fall von Alkaptonurie mit Ochronosis, München. med. Wchnschr. **59:** 364, 1912.

Ochronosis from the standpoint of the internist is best presented by Howard and Mills [22] in 1941 and is based on a world summary, unfortunately incomplete, of 55 cases.

Pomerantz [23] has found the most characteristic roentgen findings of alkaptonuric ochronosis in the spine, pelvis, shoulder and knee joints and costal cartilages. Fixation of the spine is effected by ankylosis of the vertebral bodies and their joints. The intervertebral disks are calcified and appear as elliptic opaque wafers, particularly in the lumbar areas. He believes that the density of the intervertebral disk is due to secondary calcification following degeneration of the cartilage induced by deposition of homogentisic acid.

THE EYE CHANGES IN OCHRONOSIS

A complete review of this subject does not appear in the medical or ophthalmologic literature. In the accompanying tables positive eye changes in 60 cases are shown: in 3 the changes are of undetermined origin, in 2 due to melanuria, in 20 to carbolochronosis and in 35 they are changes complicating alkaptonuria. In 18 cases the eye changes are tabulated as negative although in 14 they were not recorded or observed.

Edmund Jensen in 1904 noted the scleral pigmentation in a case but the diagnosis was not established

Scope of Tables

	Condition	Number of Cases
Table 1	Alkaptonuria	35
Table 2	Carbolochronosis	20
Table 3	Melanuria	2
Table 4	Undetermined etiology	3
Table 5	Without eye changes (negative, unrecorded or overlooked)	18
		78

until Poulsen (case 3) began his research three years later. Schultz-Zehden [24] published a short report on 2 cases in 1908. The third ophthalmologist to examine an ochronotic eye was Fleischer (Kolaczek's case 1).

The only comprehensive paper on the subject, including the first slit lamp microscopic examination, was published by Sallmann [25] in 1926. He confirmed the presence of pigment granules in the corneal periphery first observed grossly by Hecker and Wolf [26] in 1899. I shall describe this definite finding in cases 3 and 4.

Schreiber [27] described the possibility of involvement of the skin of the lid and stated that arsenic melanosis, toxic diffuse goiter and Addison's disease must be considered in differential diagnosis.

A case of conjunctival pigmentation was studied biomicroscopically by the French ophthalmologist de Cluj [28] and the gross scleral pigmentation by Anderson,[29] an Englishman, in 1937. Duke-Elder's [30] textbook is the first in the English language to mention

22. Howard, C. P., and Mills, E. S.: Ochronosis, Oxford Medicine, New York, Oxford University Press, 1941, vol. 4, pt. 1, p. 223.
23. Pomerantz, M. M.: Personal communication to the author.
24. Schultz-Zehden, P.: Die ochronosische Fleckung des Sehorgans, Klin. Monatsbl. f. Augenh. **46:** 417, 1908.
25. Sallmann, L.: Ueber die Augenpigmentierung bei endogener Ochronose, Ztschr. f. Augenh. **60:** 164, 1926.
26. Hecker, A., and Wolf, F.: Ein Fall von Ochronose, Festschr. z. Feier. d. Stadt-Krankenh. zu Dresden-Friedrichstadt, Dresden, 1899, pt. 2, pp. 325-335.
27. Schreiber, L.: Die Krankheiten der Augenlider, in von Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, ed. 3, Leipzig, Wilhelm Engelmann, 1924, p. 183.
28. Cuenod, A., and Nataf, R.: Biomicroscopie de la conjunctive, Paris, Masson et Cie, fig. 27, 1934 (Prof. Michail de Cluj).
29. Anderson, F. A.: A Note on Ochronosis, Tr. Ophth. Soc. United Kingdom **57:** part 2, 591, 1937.
30. Duke-Elder, W. S.: Text Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1766.

ochronotic pigmentation of the sclera and conjunctiva. Although Sallmann's paper is cited, no reference is made to corneal disorder.

It is now possible to evaluate the changes that may take place. The skin of the lower lids was pigmented black in 1 case (Ashburn [31]), tarsal conjunctivas and scleras were discolored in 2 (Graeffner [32] and Fleischer), pigment granules were present in the corneas and scleras in 2 (Hecker and Wolf and Sallmann), scleras and bulbar conjunctivas were pigmented in 3 (Fleischer, Poulsen and Beddard [33]), and the conjunctiva only was pigmented in 3 (Osler and Ogden,[16] de Cluj and Diebold [34]). In Sallmann's case the scleras, conjunctivas and corneas were pigmented. The scleral spots were present in 57 of the 60 cases tabulated, varying in size from that of a pinhead, a lentil seed or a bean, in shape either triangular, circular, vertical striped or like parentheses including the corneas, and in color from brown to blue or brown-black.

I have collected 23 cases (21 with eye changes) that have been omitted from previous world summaries. In every case of proved etiology reported since 1910 (except Fishberg's), eye changes were found. Formerly it was thought that ochronosis did not develop in alkaptonuria until middle age or later. Positive eye findings in Poulsen's patient at the age of 23 (and in his sixth patient at 24), de Cluj's at 25, Ashburn's at 27½, Baldwin's [35] at 31 and Kolaczek's at 30 and 35 indicate that ochronosis can be detected at an earlier age. Of ophthalmologic significance is the definite statement by Poulsen that the eyes were pigmented before the ears in his cases 3, 5, 8 and 9.

The parents of my second patient were first cousins; 3 brothers are alkaptonuric, 1 or 2 of whom have blue ears; 3 of 4 daughters are alkaptonuric and 2 showed premature calcification of the costal cartilages suggesting early ochronosis, and a grandson has alkaptonuria. This is probably the first family pedigree in which the disease is expressed as a dominant instead of a rare recessive mendelian characteristic. No treatment is known which affects the course of alkaptonuria and ochronosis except the prohibition of consanguineous marriages in affected families.

No investigator has had an opportunity to section an ochronotic globe. Pope's specimen examined grossly post mortem revealed a deposit of pigment in the superficial layers of the sclera. The microscopic finding of "ordinary fine granular pigment in the sclera," erroneously quoted in several papers, referred to the pathologist's report on the ear and rib cartilages.

Some authors have stressed the presence of dilated conjunctival vessels over the scleral spots as a factor in the production of pigment. Actually the avascularity and sluggish metabolism of the sclera accounts for the formation and storing of homogentisic acid, as occurs elsewhere in the body. Fishberg and Dolin [41] believe that the system homogentisic acid-benzoquinone acetic acid fulfils all the criteria of a reversible oxidation system. "Some light is thrown on the old question as to why the pigment in ochronosis is so strictly localized in the cartilages and scleras. Virchow states in the original description, 'I will name this condition ochronosis. It is strictly localized in those parts that are without nerves and blood vessels.' These are the regions where there can be no poising effect of hemoglobin. Hence the quinone from the homogentisic acid can be formed and at the p_H of the body fluids instantly form the colored product characteristic of ochronosis."

The localization of the scleral spots to the palpebral fissures must be related to the catalytic action of light in stimulating pigment formation in exposed areas of the body.

An authoritative work on metabolic diseases [42] in the section devoted to ochronosis does not mention eye pigmentation either as a symptom or as an aid in diagnosis. On the other hand "black sclera" is the heading found in a textbook on symptom diagnosis.[43] While this concept is extreme (only the cartilages become black), credit should be given to an American internist for attempting to classify an ophthalmologic entity.

REPORT OF CASES

CASE 1.—*History.*—B. N., a white man aged 44, a cameraman, seen Feb. 12, 1942 through the courtesy of Dr. Emanuel Stern, had no complaints about the eyes but three months previously had experienced a sensation of pain in the lower part of the lumbar region. He had corrected vision with myopic astigmatic lenses of 20/20, in both eyes. His mother and father were first cousins and the patient was born in Turkey. He stated that there was no history of alkaptonuria and that his 2 daughters and 1 son were in perfect health.

Examination.—Ophthalmologic examination showed in the palpebral fissures a conjunctival band of brownish color extending for 10 mm. temporally in the right eye and 1 mm. temporally in the left eye. By slit lamp microscopy a group of very faint pigment dots were seen near the temporal limbus at 8:30 o'clock with high power magnification. Nasally in the left eye very faint pigment dust was present in the horizontal meridian and conjunctival portion of the limbus without definite color. The changes were not sufficiently advanced to be considered pathologic.

In each ear were seen two discrete areas of blue about the hue of a dilated vein placed symmetrically near the concha and antihelix. The patient was not conscious of this abnormal coloration until it was demonstrated to him.

A laboratory examination was made at the chemical laboratory of the Hospital for Joint Diseases by Dr. Aaron Bodansky. Homogentisic acid was recovered from a specimen of urine submitted March 14. Tests for alkaptonuria gave positive results.

A report of the roentgen examination made by Dr. Maurice M. Pomerantz is as follows: "In the dorsal region, there is a moderate kyphosis. There is a distinct narrowing of all intervertebral joints with some eburnation of the articular surfaces of all vertebrae. In the lower dorsal area there is extensive calcification of the intervertebral cartilages associated with moderate hypertrophic marginal changes.

"In the lumbar area there is no unusual accentuation of the lumbar lordosis. The lumbosacral angle is definitely reduced. There is likewise distinct narrowing of all lumbar vertebrae associated with the formation of fairly large osteophytes on the anterior surface of all the segments. The articular surfaces of the vertebrae are moderately eburnated and there is some suggestion of beginning calcification of the intervertebral disks between the first and second and the fourth and fifth lumbar vertebrae.

"Examination of both shoulder girdles does not disclose any essential change in the width of either articulation. The heads of the humeri and glenoid fossae are intact. There are no calcific deposits in or about either joint.

31. Ashburn, P. M.: Alkaptonuria and Ochronosis, Mil. Surgeon **29**: 424, 1911.
32. Graeffner: Demonstration einer Kranken mit Ochronose, Berl. klin. Wchnschr. **44**: 1051, 1907.
33. Beddard, A. P.: Ochronosis Associated with Carboluria, Quart. J. Med. **3**: 329, 1909.
34. Diebold, O.: Ochronose und Unfall, Deutsche Ztschr. f. Chir. **245**: 63, 1935.
35. Baldwin, H.: A Case of Alkaptonuria, Am. J. M. Sc. **145**: 123, 1913.
41. Fishberg, Ella H., and Dolin, B. T.: The Biological Action of Strongly Positive Oxidation-Reduction Systems, J. Biol. Chem. **101**: 159 (June) 1933.
42. Duncan, G. G.: Diseases of Metabolism, Philadelphia, W. B. Saunders Company, 1942, p. 601.
43. Yater, W. M.: Symptom Diagnosis, ed. 4, New York, D. Appleton-Century Company, 1942, p. 84.

"Conclusion: The changes in the spine are those usually associated with alkaptonuria and ochronosis."

CASE 2.—*History.*—M. N., a white man aged 53, a film inspector, examined on April 22, 1941 through the courtesy of Dr. Pomerantz, is the older brother of B. N. He was also born in Turkey. Six brothers and 3 sisters are living; a seventh brother died thirty years ago following an attack of typhoid. The patient's wife states that 3 of his brothers are alkaptonuric and 1 or 2 brothers have blue ears. The patient has 4 daughters, and the 3 younger ones are alkaptonuric. A grandson aged 4 voids urine which stains diapers black.

The patient complained of pain in the shoulder joints and gave a history of vague gastric distress.

Examination.—The ears have been discolored for twenty years. The patient stands with a slight stoop and the knees flexed. There is a decided dorsal kyphosis, and lumbar lordosis is increased. There is a peculiar gray-blue discoloration of the head and neck and in numerous scattered areas over the body. The pigmentation appears to be most pronounced in the ears and about the nose.

All tests for alkaptonuria gave positive results;[43a] the Wassermann reaction was negative.

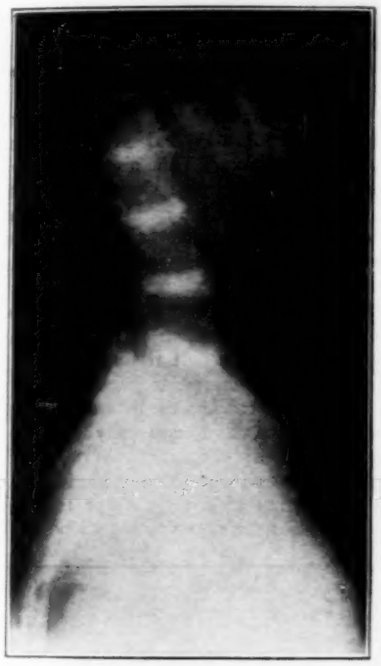

Fig. 2 (case 2).—Characteristic calcification of the intervertebral cartilages observed in all cases in the series.

Roentgenograms show narrowing of the shoulder joints with considerable eburnation of the head of the humerus and glenoid. There is narrowing of the intervertebral joints with calcification of the cartilage and extensive calcification of the costal cartilages. The lateral view shows calcification of the intervertebral cartilages and spinal ligaments posteriorly. Roentgenograms of 2 daughters reveal intense premature calcification of the costal cartilages.

Vision in both eyes is 20/20 with hyperopic correcting lenses. A faint yellow-brown conjunctival discoloration is present in the palpebral fissures extending 5 mm. temporally from the limbus and nasally in each eye 3 mm. from the limbus. The nasal discolorations are of a lighter hue and the left is more diffuse and browner than the right.

Slit lamp examination showed that the corneas are normal. One discrete, dark brown pigmented dot was seen in the left limbus conjunctiva. Examination otherwise was negative; no pigmentation was present in the conjunctiva or sclera and the faint staining seen grossly appeared related to increased color intensity in the pingueculae.

The ears are a slate gray-blue and are unduly rigid. The cartilages appeared opaque by transillumination.

CASE 3.—*History.*—H. G., aged 65, a former bank messenger, was admitted to the Third (New York University) Medical Division, Welfare Hospital, service of Dr. J. Murray Steele, on July 14, 1939.

The patient had sustained a skull fracture in 1929 and a fracture of the lower third of the right femur in 1939. Between 1929 and 1939 he had been hospitalized four times at various institutions, and the diagnosis of ochronosis had not been made. The diagnosis on admission was malunion of a fractured right femur. In 1932 an iridectomy and a cataract extraction were performed on the right eye and the same operations were performed on the left eye one year later. At this time the ophthalmologist called the patient's attention to a colored spot in the left eye.

The family history was negative.

Examination.—The urine turned dark brown to black on standing, a change which developed almost instantly following the addition of ammonia water. Benedict's solution reduced dark green with yellow precipitate formation; alkapton bodies were present.

Fig. 3 (case 3).—Temporal ochronotic spot of average size (3 mm. by 5 mm.) in alkaptonuria of long standing (depression of frontal bone after skull fracture).

On physical examination there was a faint cyanotic tint in both ears and transillumination revealed diffuse pigmentation of the aural cartilages, as noted in case 2.

Fig. 4 (case 3).—Same characteristics of intervertebral cartilages shown in figure 2.

Ascorbic acid was given to the patient in an attempt to influence the excretion of homogentisic acid, without effect. These experiments have been reported by Sealock, Galdston and Steele.[44] Other vitamins were given to the patient without affecting the output of homogentisic acid.

43a. Fishberg, Ella H.: The Instantaneous Diagnosis of Alkatonuria on a Single Drop of Urine, J. A. M. A. **119:** 882 (July 11) 1942.

44. Sealock, R. R.; Galdston, M., and Steele, J. M. Administration of Ascorbic Acid to an Alkaptonuric Patient, Proc. Soc. Exper. Biol. & Med. **44:** 580. 1940.

Roentgen examination was done by Dr. Henry K. Taylor and showed hypertrophic arthritis of the shoulders and spine, intervertebral disks almost completely obliterated and considerable decalcification of the spine; the right hip showed almost complete absorption of the head of the femur; the neck formed an articulation with the acetabular shelf; prostatic calculi were present. There was considerable calcification of the vessels of the legs and a calcareous plaque in the aortic arch.

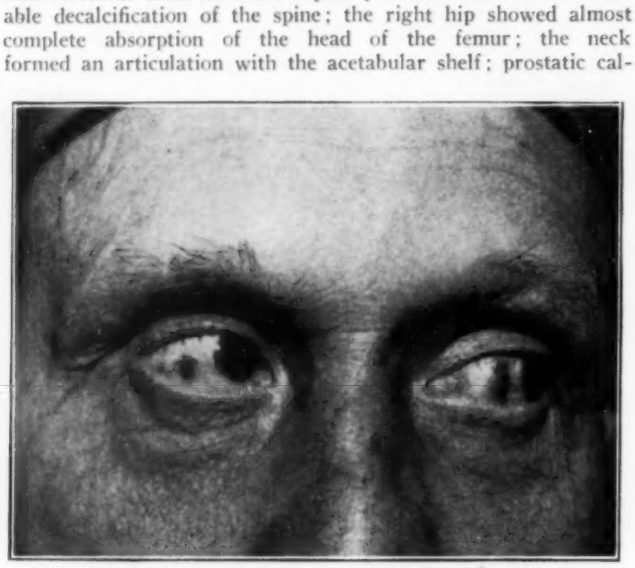

Fig. 5 (case 4).—Pigmentation of scleras in alkaptonuric ochronosis. The left lesion nasally is unusual in length and is partly covered by the eyelids.

With the aphakic lens corrected vision of the right eye is 20/20 minus and of the left eye 20/40. A faint secondary cataractous membrane accounts for subnormal vision in the left eye. The fundi are grossly normal. Transillumination of the sclera suggests some thinning at the sites of insertion of the external rectus tendons.

Slit Lamp Biomicroscopy—Right Cornea: One and five-tenths mm. from the temporal limbus three brown pigment spots are situated very superficially, probably just beneath Bowman's membrane; a single larger pigment dot is seen beneath the conjunctival layer of the cornea. No pigmentation is present nasally. A defect in Descemet's membrane is noted at 5 o'clock. The posterior third of the cornea is pigmented, probably of traumatic origin after the cataract extraction.

Right Sclera: Three mm. temporal from the limbus a slate gray purplish area 2.5 mm. wide and 6 mm. high is seen between 8 and 10 o'clock levels of the cornea, situated superficially in the sclera. By slit lamp examination brown pigmentation appears under the conjunctival vessels. The pigment is filamentous or spiral and some areas simulate incompletely closed rings. The pigment is not arranged in clumps or groups as portrayed in the drawing of de Cluj reproduced in Duke-Elder's textbook.

Three mm. nasal from the limbus a faint gray area 2 mm. wide and 5 mm. high is seen between the 3 and the 5 o'clock level of the cornea situated more superficially in the sclera and pigmented a brownish yellow in the slit lamp beam.

A 5 mm. zone of sclera beyond the limbus appears light blue. The remainder of the sclera externally is normal, although transillumination suggests uniform thinning.

Left Cornea: Temporally eight fine round, brownish yellow spots are seen posterior to the fine limbus conjunctival vessels in the substance of the cornea. Nasally, 2 mm. from the limbus in the 9 o'clock meridian two tiny pigmented spots appear just behind Bowman's membrane.

Left Sclera: Three mm. temporal from the limbus a slate gray purple area 3 by 5 mm. surrounded by a pink border of blood vessels is seen between the 2 and the 4 o'clock level of the cornea. A similar distance from the cornea nasally a small faint blue area 1 by 2.5 mm. appears between the 9 and the 9:30 level of the cornea. Slit lamp microscopy reveals the same brown spiral and ringlike pigmentation as was noted in the right sclera. The conjunctiva moves over the scleral areas during the winking reflex and does not appear to be involved.

CASE 4.—*History.*—F. D., a cigar maker aged 61 when admitted to the Welfare Hospital on June 10, 1940, service of Dr. J. Murray Steele, had previously been studied in the service of Dr. I. O. Woodruff at Bellevue Hospital, and the roentgen findings were reported by Pomerantz, Friedman and Tunick.[45]

The patient's father died of unknown causes many years ago and his mother died of pneumonia at the age of 58. Two brothers and 1 sister are alive and well. There is no history of consanguinity and no other member of the family has suffered from alkaptonuria.

He had amaurosis of the left eye following recurring attacks of iritis after an injury in 1918. During the past eighteen years he has suffered from severe pain in the lower part of the back. Later he experienced pain and stiffness in the shoulders and right knee which are now so intense as to be almost completely disabling. The patient walked with a great deal of difficulty, had limited range of motion at the knees and could not abduct his arms. He stated that for thirty-five years he had noted a bluish discoloration of the ears but that he had never observed anything peculiar in the color of the urine. For the past thirty-six years he has observed yellow discoloration of the right palpebral fissure temporally, and in the left fissure nasally. Prominent dark spots in the scleras were observed by his friends about six years before admission.

Examination.—The patient's spine appears fixed. His head is thrust forward and the arms hang limply at his sides. The knees are flexed. The skin, particularly on the head, neck and chest, shows peculiar mottled bluish and in some areas brownish pigmentation or discoloration. This pigmentation is most noticeable in the ears and at the tip of the nose. In the region of the small joints, particularly of the hands, are peculiar bluish linear discolorations which seem to be beneath the skin.

Roentgen examination showed narrowing of the vertebral articulations with extensive calcification of intervertebral cartilages; peculiar granular osteoporosis and ankylosis of the spine, with loss of normal curves; calcification of the interpubic cartilage with similar depositions in the soft tissues of the hip joints; partial synosteosis of the right sacroiliac joint and fusion of the lumbar spinous processes; calcareous deposits in the patella tendon and popliteal space, and unusually advanced Mönckeberg's arteriosclerosis. Roentgenograms of the ears revealed the presence of opaque deposits simulating gouty tophi.

Ophthalmologic Findings: Vision of the right eye is 20/15 and the left eye is blind following recurring specific iridocyclitis starting in 1917. Ophthalmoscopic examination shows the media to be clear, with physiologic excavation of the optic nerve prominent and retinal arteriosclerosis. In the blind eye there are numerous posterior synechiae following recurring attacks of iritis, probably of specific origin. Glaucomatous excavation of the optic nerve and retinal arteriosclerosis are seen. The clinical diagnosis was amaurosis following secondary glaucoma.

Fig. 6 (case 4).—Showing the right nasal and left temporal scleral spots. The mottled pigmentation of the skin of the nose is apparent.

45. Pomerantz, M. M.; Friedman, L. J., and Tunick, I. S.: Roentgen Findings in Alkaptonuric Ochronosis, Radiology **37**: 295 (Sept.) 1941.

Slit Lamp Biomicroscopy.—Right Cornea: In a zone 0.5 to 2 mm. inside of the temporal limbus are seen groups of oval pigment spots situated in the superficial layers. The spots are darker brown and larger than the ones in the cornea in case 3. Four spots of pinhead size are present at 9:30 o'clock; toward 7 o'clock there are five more, and inferiorly are scattered many smaller and finer ones. The periphery of the cornea at 9:30 is opaque. At the limbus is a groove 2 mm. vertical and 1 mm. horizontal resembling marginal atrophy. The thickness of the cornea is decreased about one half at this point. In a zone 2.5 mm. inside the nasal limbus between 2:30 and 4:30 o'clock are nine large and many powder grain dark brown spots.

Right Sclera: Five mm. temporal from the cornea a slate purplish area 2 mm. wide and 5 mm. high is seen surrounded on each side by injected conjunctival vessels. The upper edge lies opposite the 9 o'clock corneal level while the inferior edge extends lower than 7 o'clock level and is covered by the lower lid. Pigmentation of the conjunctiva is not seen microscopically. The slate gray change is definitely in the sclera. The subconjunctival vessels are not increased in number over that seen normally in the palpebral fissure or about a pinguecula of an aged patient. A thinning of the sclera is suggested in this area.

Four mm. nasal from the limbus is seen a triangular purplish slate gray area measuring 9 mm. high, 6 mm. at the widest point, tapering to 2 mm. superiorly and 1 mm. inferiorly and lying between the 1 and 4 o'clock levels of the cornea. The conjunctival vessels are injected along the nasal border. Pigmentation of the conjunctiva is not seen microscopically. The slate gray area lies beneath the conjunctiva, which moves freely above it. Episcleral blood vessels are increased over those seen in a normal eye.

Left Cornea: The pigment spots are so numerous that they can be seen without magnification. Near the temporal limbus about thirty dark brown spots are noted, some pinhead size and others as small as powder grains. They are located in the most superficial layers of the cornea, probably just below Bowman's membrane. Several appear like droplets, and a convex reflection is seen suggesting that some of the pigment spots have a different refractive index.

Near the nasal limbus about thirty-five spots are seen, also of varying sizes. Some lie deep but most of the pigmented areas are in the superficial layers of the cornea.

Left Sclera: Five mm. temporal from the limbus is seen a slate gray area measuring 2 by 5 mm. surrounded by faint conjunctival injection lying between the 3 and the 6 o'clock level of the cornea. The conjunctiva is not pigmented and the number of conjunctival and episcleral vessels are increased over normal.

The most prominent ochronotic patch is seen 3 mm. nasal from the limbus of slate gray and is devoid of the purple hue noted in the right sclera nasally. It measures 5 mm. wide in the middle third, 3 mm. in the upper and lower thirds and 10 mm. high. The upper edge corresponding to the 11 o'clock corneal level is covered by the upper lid, and the inferior edge extending lower than the 6 o'clock meridian is well covered by the lower lid. The temporal and nasal edges are surrounded by injected conjunctival vessels. The pinguecula lies in front of the colored scleral zone. Microscopically the conjunctiva is unpigmented. The sclera is diffusely colored a slate gray. Grouped pigmentation is not seen. The scleral sites nasally and temporally seem indented, suggesting thinning of these areas.

The distribution of pigment in the four scleral areas followed a similar pattern. In the center it appeared darker and mounted. At the periphery the slate areas changed in color from brown to yellow and imperceptibly into adjoining normal sclera.

DIFFERENTIAL DIAGNOSIS

In melanosis bulbi small flecks or large islands of dense slate blue or brown pigmentation appear in the sclera. The sites involved are not limited to the palpebral fissure. Basil Graves [46] and Culler [47] described scleral plaques near the nasal limbi in patients over 60 years of age which vary in size from pinpoint to approximately 2 mm. in the horizontal plane and 6 mm. in the vertical plane. They are slate gray because the ciliary body shows through the area of increased transparency. Pillat [48] has reported a senile degeneration of the sclera over the tendinous insertions of the rectus muscles which appears as a dark band of dirty gray. He does not believe that the finding is related to pigmentation of the bulbar conjunctiva, as seen in arsenic melanosis, ochronosis or Addison's disease. Scleral ochronosis is readily differentiated by its superficial localization in the palpebral fissures temporally and nasally. The progressive color changes from faint brown to slate blue or black when associated with blue ears, alkaptonuria and definite roentgenographic changes establishes the diagnosis beyond question.

Fig. 7 (case 4).—In addition to the points mentioned in legend for figures 2 and 4 there is likewise well defined osteoporosis and slight hypertrophic changes are present at the margins of all the vertebrae.

The occasional involvement of the skin of the lid may suggest the bronzelike pigmentation of Addison's disease or the dark discoloration associated with generalized argyrosis.

In the conjunctiva by slit lamp microscopy the brown pigment, when present, appears subepithelial, like cystic dilatations near the borders of the scleral spots, and is deposited in crescent, spiral or open ring formations. Congenital pigment flecks which sometimes increase in size and the fine granular epithelial and subepithelial pigment seen in Addison's disease do not present the same microscopic picture.

The corneal involvement is characteristic. The presence in the superficial layers near the temporal and nasal limbi of discrete brown pigment spots which by retroillumination appear like oil droplets on water cannot be confused with any other slit lamp biomicroscopic finding.

46. Graves, Basil: Bilateral Mesial Superficial Deficiency of the Sclera, Brit. J. Ophth. **21**: 534, 1937; Bilateral Mesial Superficial "Deficiency" of the Sclera (Scleral Plaques), ibid. **23**: 191, 1939.

47. Culler, A. M.: The Pathology of Scleral Plaques, Brit. J. Ophth. **23**: 44, 1939.

48. Pillat, A.: Concerning a Peculiar Senile Degeneration of the Sclera Over the Site of Insertion of the Rectus Muscles, Ztschr. f. Augenh. **82**: 113, 1933-1934.

SUMMARY

The total number of cases of ochronosis in the literature has been increased to 82 by the addition of 23 omitted from previous reviews and the 4 cases reported here from the ophthalmologic angle.

Alkaptonuria is a relatively common disease. Endogenous alkaptonuric patients may exhibit signs of ochronosis before the age of 30.

The diagnostic triad in ochronosis is pigmentation of the ears and scleras, urine that darkens on exposure to air and osteoarthritis.

CONCLUSION

Ocular ochronosis was found as a complication in every proved case but 1 since 1910.

Pigment spots in the corneas superficially near the temporal and nasal limbi represent a slit lamp biomicroscopic finding which is diagnostic of advanced ochronosis.

Scleral ochronosis develops gradually and simultaneously with pigmentation of the ear cartilages or may be one of the first signs of ochronosis.

Careful ophthalmologic study should reveal abnormal pigmentation of the scleras or conjunctivas in patients seen early and pigment spots in the corneas in alkaptonuric patients past middle age.

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ABSTRACT OF DISCUSSION

Dr. M. L. Berliner, Brooklyn: In a case which I examined the conjunctival pigmentation was seen in the form of ovular brownish spots which under high power were composed of granules in a partially closed ring arrangement. The appearance and disposition of the pigment in the cornea are typical. It is found in Bowman's zone as small brownish discrete globules, resembling oil droplets symmetrically arranged. It would be interesting to speculate on whether the pigment migrates along the basal cell layers of the conjunctival epithelium into the cornea or whether it arises in situ. The fact that the pigment tends to develop in the nearly avascular tissues such as tendons and cartilages might cause one to favor the latter idea. Although alkaptonuria is a symptom of ochronosis, it may occur as an isolated finding. Two types of ochronosis are known: (1) the endogenous form, an inherited metabolic anomaly associated with alkaptonuria, and (2) the exogenous form, resulting from phenol (carbolo-ochronosis) or benzene poisoning, including such substances as dinitrophenol, paradichlorobenzene, aniline, epinephrine and similar aromatic compounds. All these when ingested tend to form phenol derivatives in their intermediate metabolism. These intermediate products at the slightly alkaline p_H of the body fluids polymerize into pigments. An analogous reaction occurs with epinephrine solution, which when left exposed to air turns dark. In the first or endogenous group (represented by Dr. Smith's cases), there is a total inability to destroy tyrosine and phenylalanine contained in the proteins of food and tissues, resulting in the excretion of homogentisic acid, an intermediary product. This substance is excreted into the urine. After many years as the result of the action of tyrosinase there is a deposition of a black pigment similar to melanin in the cartilages and tendons. I reported 2 cases of cataract from poisoning by inhalation of paradichlorobenzene vapor (a commonly used moth repellant). In 1 of these cases phenol derivatives were found in the urine. The urine turned dark on standing. Several months after the patients were removed from the action of the fumes they suddenly acquired cataracts. The posterior cortex of the lens of a woman aged 30 became definitely dark brown of the so-called nigra type. This was followed by a rapid swelling of the cortex. I would suggest that biochemical studies of tissues and excretions be made in such cases as black cataracts, melanosis oculi, whorl-like keratitis, Hudson's line and others which are characterized by melanin or melanin-like pigmentation.

Dr. James W. Smith, New York: A pocket flashlight held behind the ear will delineate the opaque cartilage, affording a simple clinical diagnostic test. The ochronotic areas cannot be transilluminated. The cases of orchronosis known definitely to be of alkaptonuric origin total 45. Of these 31 (69 per cent) occurred in males and 14 (31 per cent) in females. This finding contrasts with statements in the literature that the sex incidence is about equal in men and in women. Many cases of alkaptonuria and ocular ochronosis were never recorded. In the family of my second patient alone there are 5 with alkaptonuria and potential ochronosis not yet investigated. It is important to remember that the eye picture is variable and progressive, starting as a faint, diffuse, brown discoloration in the palpebral fissure and ending as a slate colored and conspicuous brown-black scleral spot. I arranged my 4 cases chronologically in order to demonstrate this point. The ophthalmologist should be able to aid the internist in detecting ochronosis by slit lamp examination of young adults. There is a possibility that some day homogentisic acid may be recovered from tears just as it can now be detected in urine. Every case of alkaptonuria at birth is a potential case of ochronosis. By roentgenographic examination cases can be diagnosed in the second decade or possibly even sooner. Sealock, Gladston and Steele have suggested that the continued high intake of vitamin C in early life may prevent the deposition of melanotic pigment in later years.

IRREGULAR ISOAGGLUTININS

ISRAEL DAVIDSOHN, M.D.

CHICAGO

The concept of what constitutes irregular isoagglutinins has undergone profound changes during the last forty years. Isoagglutination means clumping of red cells by serum or plasma of an individual of the same species; isoagglutinins are the clumping antibodies in the serum. Heteroagglutination or clumping of red cells by serum of an individual of another species has been known at least since 1874, when Landois published a monograph on blood transfusion.[1] It seemed natural that bloods of different species should manifest incompatibility, but the observation by Landsteiner[2] in 1900 of clumping in a mixture of bloods of two healthy human beings was a surprise, especially since it was noted in some combinations of bloods and not in others. Actually a number of publications which followed Landsteiner's original report referred to isoagglutination as a manifestation of disease. Some writers were quite certain that it never occurs in health,[3] others conceded that it may occur in an occasional normal individual, though as a rule it is abnormal.[4] Later investigations confirmed Landsteiner's original concept of isoagglutination as a normal physiologic phenomenon.

According to Landsteiner, every person has in his serum agglutinins for the agglutinogens which he lacks in his blood. The formulas of the four blood groups

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Read before the Section on Pathology and Physiology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

1. Landois, L.: Die Transfusion des Blutes, Leipzig, S. C. W. Vogel, 1875.

2. Landsteiner, Karl: Zur Kenntnis der antifermentativen, lytischen und agglutinierenden Wirkungen des Blutserums and der Lymphe, Zentralbl. f. Bakt. **27**: 357 (Feb. 10) 1900.

3. Grünbaum: Agglutination of Red Corpuscles, Transactions of the Liverpool Medical Institution (Path. and Micr. Section) April 19, 1900. Brit. M. J. **1**: 1089 (May 5) 1940. Eisenberg, Philip: Ueber Isoagglutinine und Isolysine in menschlichen Soris, Wien. klin. Wchnschr. **14**: 1020 (Oct. 17) 1901.

4. Donath, J.: Zur Kenntnis der agglutinierenden Fähigkeiten des menschlichen Blutserums, Wien. klin. Wchnschr. **13**: 497 (May 31) 1900. Ascoli, M.: Isoagglutinine und Isolysine menschlicher Blutsera, München. med. Wchnschr., July 30, 1901, p. 1239.

are O (anti A, anti B), A (anti B), B (anti A) and AB (o).

What then are irregular isoagglutinins? One could define them as isoagglutinins which are not found regularly in the normal pattern of blood groups and types. The term type is used for blood factors other than A and B, for instance for the properties M and N.

Several deviations from the previously mentioned formulas are known, some of practical importance. One of them is based on the discovery made by von Dungern and Hirszfeld in 1911 that the agglutinogen A occurs in two forms, a strongly agglutinable A_1 and a weakly agglutinable A_2. About four fifths of group A and AB bloods have the stronger A_1 factor; the rest have the weaker A_2 factor. As a result, four subgroups have been recognized: A_1, A_2, A_1B and A_2B. Recently a still weaker form of group A has been demonstrated, subgroup A_3. A voluminous literature has accumulated on the question of whether these subgroups represent merely quantitative or qualitative differences. The proponents of a qualitative nature of the differences seem to have the better of the argument. In connection with the subject under discussion it is of interest that there are occasionally so-called irregular isoagglutinins in these subgroups reacting with the A factor of the other variety. The rare agglutinin in the serum of the subgroup A_2 or A_2B clumps red cells of subgroup A_1 or A_1B and is known as the a_1 agglutinin. The still more infrequent agglutinin in subgroup A_1 or A_1B agglutinates red cells of subgroup A_2 and A_2B and is called a_2. The latter agglutinin has the further unusual property that it clumps the normally inagglutinable group O. According to some, the a_2 agglutinin is reacting specifically with the factor O and with A_2 only because A_2 is as a rule heterozygous and as such contains the recessive O factor. The practical significance of these two irregular agglutinins is that they may lead to confusion in blood grouping and cross matching tests. It was shown that a_1 and a_2 react best at temperatures between 15 and 18 C. and therefore belong to the group of so-called cold agglutinins to be discussed later. However, they may react even at body temperature, as will be shown later.

The following case report illustrates occasional difficulties due to such irregular agglutinins. An anemic patient with a history of periodic hemorrhages from the gastrointestinal tract, the exact nature of which was not established at the time of this study and who had previously received nineteen uneventful blood transfusions, needed another transfusion. It was found in the laboratory of Dr. A. S. Giordano of South Bend, Ind., that the patient's blood was of group A but that his serum clumped red cells of a donor of group A and of several donors of group O.

The red cells of the patient were determined as belonging to subgroup A_1 and as Rh positive. The determination of the subgroup was done according to the method of the author [5] in which an immune serum is obtained from rabbits treated with boiled red cells of sheep. This serum differentiates the subgroups A_1, A_2, A_1B and A_2B very sharply by clumping red cells of all subgroups in lower dilutions and only A_1 and A_1B in higher dilutions. The dilutions to be used have to be determined by titrations. High titered immune serums are easily produced and keep well.

From the accompanying table it is apparent that the reason for the difficulty in blood grouping was the presence of the a_2 agglutinin. This agglutinin clumped cells A_2 and O equally strongly not only at room temperature but also at 37 C. The titer was 1:3 at room temperature and 1:1.5 at body temperature. The titer of the anti B agglutinin was 1:12. Another specimen obtained about one month later reacted similarly.

Adsorption of the serums with A_2 cells removed agglutinins for A_2 and O cells and adsorption with O cells had the same effect. It is of interest that the a_2 agglutinin reacted at body temperature, while as a rule it reacts only at lower temperatures. Only a donor of subgroup A_1 would be suitable for this patient.

Reaction of Patient with a_2 Isoagglutinin

	Serums							
	Group			Sub-grouping *		Human Anti Rh		
Cells	A	B	O	1:25	1:150	1	2	3
Patient	—	+	+	+	+	+	+	+
Controls								
O Rh positive	—	—	—	—	—	+	+	+
O Rh negative	—	—	—	—	—	—	—	—
A_1 Rh positive	—	+	+	+	+	+	+	+
A_2 Rh negative	—	+	+	+	—	—	—	—

Result: Patient's cells (P) = A_1 Rh positive

	Known Cells							
Serums	A_1	A_2	B	O	O Rh Positive	O Rh Negative	A_1 Rh Positive	A_2 Rh Negative
Patient	—	+	+	+	+	+	—	+
Controls								
A	—	—	+	—	—	—	—	—
B	+	+	—	—	—	—	+	+
O	+	+	+	—	—	—	+	+
Anti Rh 1	..	..	..	..	+	—	+	—
Anti Rh 2	..	..	..	..	+	—	+	—
Anti Rh 3	..	..	..	..	+	—	+	—

Result: Patient's serum (P) has a_2 in addition to anti B
Patient's blood formula: A_1 Rh positive anti B a_2

* Subgrouping serum = immune serum produced by injections of boiled sheep blood.

+ indicates presence of agglutination; —, absence of agglutination.

The a_1 and a_2 isoagglutinins are not in disagreement with the law of Landsteiner as quoted, since the evidence favors the concept of a qualitative difference between A_1 and A_2.

Another type of difficulty and the manner in which it was solved is presented in the report of the next case: [6] A 2½ year old Negro boy with tuberculosis and a positive complement fixation reaction for syphilis required a blood transfusion, but there were difficulties in selecting a suitable donor because the boy's serum clumped red cells of his own group and of group O. Dr. Elizabeth Schirmer kindly submitted the blood to me. I found that the patient's red cells were of group A, subgroup A_1, type N and Rh positive and that his serum clumped red cells of subgroups A_1 and A_2 and of group O rather irregularly. The bloods of some individuals of these groups and subgroups were clumped and those of others were not. There was no extreme difference between the reactions at 0 to 5 C. and at 22 C., but at 37 C. the reactions were weaker

5. Davidsohn, Israel: A Method for Recognition of Blood Subgroups A_1 and A_2, J. A. M. A. **112**: 713 (Feb. 25) 1939.

6. Davidsohn, Israel, and Schirmer, Elizabeth: Normal Anti M Isoagglutinins: A Case Report, Proc. Chicago Path. Soc., Oct. 13, 1941.

though distinct. It was found that all the cells that were agglutinated by the serum had one thing in common: the factor M. By proper adsorptions it was demonstrated that the formula of the blood was A_1N Rh positive anti B anti M. It is characteristic for the M and N blood types that there are no normal agglutinins for them in human serum. Only 4 instances of anti M agglutinins in man have been reported previously, the latest by Wiener and Forer.[7] Two specimens of blood were obtained subsequently, one eight months and the other twelve months after the first examination. The first specimen still contained the anti M agglutinins, though in a lower titer; the specimen obtained after twelve months showed a minute trace detectable only at room temperature but not at body temperature. The parents were both of type N and had no anti M agglutinins.

The origin and nature of the irregular a_1, a_2 and anti M isoagglutinins are unknown, just as are the origin and nature of the so-called normal isoagglutinins anti A and anti B, although there is no lack of hypotheses attempting to explain the origin of the latter.

The next group of irregular isoagglutinins is the cause of serious and even fatal, now frequently preventable, blood transfusion reactions. They are due to isoimmunization of a person by a blood factor which is absent from his blood and is introduced parenterally. The story of the discoveries of the Rh factor by Landsteiner and Wiener,[8] of the role of isoimmunization by this factor in intragroup transfusion reactions by Wiener,[9] of the isoimmunization by the Rh factor in pregnancy and of its role in transfusion reactions in pregnancy and in the pathogenesis of erythroblastosis fetalis by Levine [10] is one of the notable events in recent scientific developments. The hypothesis of Levine was confirmed by Potter, Davidsohn and Crunden.[11]

The existence of qualitative differences in the Rh agglutinogens in human Rh positive blood was first established by Wiener;[12] similar differences in the Rh property in the bloods of man and the rhesus monkey were reported by Landsteiner and Wiener.[13] Toharsky and I [14] furnished experimental evidence to the effect that the Rh factor in man consists of several fractions and that the factor in man and in the rhesus monkey are not identical.

Related to this group are rare instances of isoimmunization of persons of subgroup A_1 who receive the blood of subgroup A_2, or vice versa. That subgroups A_1 and A_2, A_1B and A_2B are not always compatible was claimed by some writers and denied by others.[8] A recent publication by Wiener [15] records instances of immune isoagglutinins against subgroups A_1 and A_2, as contrasted with the rare, normal, not immune a_1 and a_2 agglutinins.

Cold agglutinins are another form of irregular isoagglutinins. They react as a rule with red cells of all groups, even with the cells of the same individual. In most instances they are active only at ice box temperature, but sometimes even at 20 to 22 C. (room temperature), and then they frequently display a certain degree of specificity and react only with the cells of some persons. This form of agglutination is a true agglutination, a true antigen-antibody reaction, as contrasted with pseudoagglutination, the most common example of which is rouleau formation. The antibody responsible for cold agglutination can be removed by adsorption. With pseudoagglutination, treatment of serum with red cells does not alter the ability of the serum to form rouleaux.

The titer of cold agglutinins may be fairly high at ice box temperature but it drops rapidly as the temperature rises and is only rarely demonstrable at 20 C. and still rarer at 37 C. It may be a source of error in blood grouping and in cross matching tests, as in the case of an 8 year old boy of group A with tuberculosis of a hip who had received several blood transfusions without reactions. One day his blood was compatible with donors of group A, but suddenly the next day it was found incompatible with that of several donors of groups O and A; among the latter was one who had given blood to the patient on two previous occasions. Dr. A. S. Giordano sent me the blood of the patient and of the donor who had been compatible on a previous occasion and who became suddenly incompatible. Both were found to be of subgroup A_2. The donor's serum showed no abnormalities, but the serum of the patient clumped indiscriminately red cells of all groups and also the cells of the donor and the patient's own cells at 0 to 5 C. At 22 C. the serum behaved similarly but did not clump its own cells and the cells of the donor, whereas at 37 C. it behaved as would be normal for its group. This was then an instance of cold agglutinins of a rather wide thermal range, leading to difficulties in cross matching tests. The examination at 37 C. cleared up the difficulty, as it does in most instances. The failure of the serum to clump the cells of the donor at 22 C., although it did clump the cells of the same donor twenty-four hours earlier in South Bend, can be explained by deterioration of the cells in transport, which is known to decrease their sensitivity.

It is generally denied that so-called cold agglutinins can be responsible for blood transfusion reactions. I have studied instances of such reactions in which all other possible causes were eliminated but in which strong cold agglutinins reacting at room temperature were present. In some instances special conditions like abnormalities in the blood of the patient were observed. In a recent transfusion reaction the connection between cold agglutinins and a hemolytic reaction seemed sug-

7. Wiener, A. S., and Forer, S.: A Human Serum Containing Four Distinct Isoagglutinins, Proc. Soc. Exper. Biol. & Med. **47:** 215 (June) 1941.

8. Landsteiner, Karl, and Wiener, A. S.: An Agglutinable Factor in Human Blood Recognized by Immune Serums for Rhesus Blood, Proc. Soc. Exper. Biol. & Med. **43:** 223 (Jan.) 1940.

9. Wiener, A. S., and Peters, H. R.: Hemolytic Reactions Following Transfusions of Blood of the Homologous Groups, with Three Cases in Which the Same Agglutinogen Was Responsible, Ann. Int. Med. **13:** 2306 (June) 1940.

10. Levine, Philip, and Stetson, R. E.: An Unusual Case of Intragroup Agglutination, J. A. M. A. **113:** 126 (July 8) 1939. Levine, Philip; Katzin, E. M., and Burnham, Lyman: Isoimmunization in Pregnancy: Its Possible Bearing on the Etiology of Erythroblastosis Fetalis, ibid. **116:** 825 (March 1) 1941. Levine, Philip; Burnham, Lyman; Katzin, E. M., and Vogel, Peter: The Role of Isoimmunization in the Pathogenesis of Erythroblastosis Fetalis, Am. J. Obst. & Gynec. **42:** 925 (Dec.) 1941.

11. Potter, E. L.; Davidsohn, Israel, and Crunden, A. B.: The Importance of the Rh Blood Factor in Erythroblastosis, Am. J. Obst. & Gynec., to be published.

12. Wiener, A. S.: Hemolytic Reactions Following Transfusions of Blood of the Homologous Group: II. Further Observations on the Role of Property Rh, Particularly in Cases Without Demonstrable Isoantibodies, Arch. Path. **32:** 227 (Aug.) 1941.

13. Landsteiner, Karl, and Wiener, A. S.: Studies on an Agglutinogen (Rh) in Human Blood Reacting with Anti Rhesus Serums and with Human Isoantibodies, J. Exper. Med. **74:** 309 (Oct.) 1941.

14. Davidsohn, Israel, and Toharsky, B.: The Rh Factor; an Antigenic Analysis, Proc. Chicago Path. Soc., Feb. 9, 1942; Am. J. Clin. Path. **12:** 434 (Aug.) 1942.

15. Wiener, A. S.: Subdivisions of Group A and Group AB: II. Immunization of A_2 Individuals Against A_1 Blood; with Special Reference to the Role of the Subgroups in Transfusion Reactions, J. Immunol. **41:** 181 (June) 1941.

gestive. A 4½ year old girl, a patient of Dr. H. G. Poncher, who is separately reporting this case with its many unusual features, suffered from hemolytic jaundice. She was of group O and received several uneventful transfusions but had a severe hemolytic reaction with oliguria following a transfusion with blood of the same group selected with meticulous care. Examination by me showed that the patient was Rh negative and had anti Rh agglutinins, and the donor whose blood caused the reaction as well as several of the previous donors was Rh positive. This then was an example of isoimmunization of an Rh negative person by previous transfusions of Rh positive blood. The child recovered from the reaction and received during the following month repeated transfusions from carefully selected Rh negative donors. The child had received altogether 2,500 cc. of Rh negative blood without any untoward reactions when one day, after the injection of about 250 cc. of Rh negative blood, she became pale, trembling and lethargic, had severe chills, her temperature rose to 105 F. in one hour and two to three hours afterward she had a definite hemoglobinuria. The child recovered. The record showed that the child's serum had cold agglutinins for the cells of the donor reacting strongly at 5 C. and weakly but distinctly at 22 C. but not at 37 C. The blood of the donor was kept in the ice box for twenty-four hours and then at room temperature approximately forty minutes before the transfusion was started. The blood was given at the rate of 30 to 35 drops a minute.

It seems to me that with cold agglutinins of the wide thermal range present in the patient's blood and clumping the blood of the donor in the test tube at 22 C. and with the transfused blood having a temperature probably lower and certainly not higher than room temperature, the conditions were present for a hemolytic reaction.

It is possible that changes in the condition of the red cells may be a factor which can influence the action of the so-called cold agglutinins. It is of interest that Landsteiner and Witt considered that possibility in a paper published in 1924.[16] The opinion that agglutinins acting at lower than body temperatures may be disregarded is contradicted by the practice of pretransfusion tests in which blood grouping and cross matching tests are done at room temperatures, and conclusions are drawn from these tests regarding a process that takes place at body temperature.

I am fully aware of the fact that, according to the prevalent opinion, so-called cold agglutinins play no part in untoward transfusion reactions. However, it is well to remember that this opinion goes back to a time when stored blood kept in refrigerators was not used for transfusions and when the occurrence of so-called cold agglutinins of a rather wide thermal range of reactivity and of a limited specificity was not known. I am not at all certain that statements in recent publications to the effect that blood stored in refrigerators may be injected without any attempt to raise its temperature should be endorsed as a safe procedure.

There is a special form of cold agglutinins known as autoagglutinins and found occasionally in patients with diseases of the liver and of the blood vessels, in trypanosomiasis and in other diseases. There are instances of this type of antibody in persons free of any evidences of disease. I studied recently the blood of a woman with a condition resembling Raynaud's disease. The abnormality of the blood became apparent when it was found impossible to do a blood count because the cells clumped in the diluting fluid. The serum of the patient agglutinated cells of all groups including her own red cells at ice box temperature and at 22 C. but behaved at 37 C. like a normal serum of group B. The same was true for the patient's red cells, which were clumped at the two lower temperatures even when suspended in saline solution. When the cells of the patient were washed three times with isotonic solution of sodium chloride they lost their abnormal behavior.

Wiener [17] reported recently an observation of autoagglutinin reacting even at body temperature.

The fourth type of irregular isoagglutination is due to action of certain bacteria on red blood cells. It is known as the Thomsen phenomenon.[18] A variety of bacteria, most of them nonpathogenic, were found by Friedenreich and others to bring about a change in red cells, making them panagglutinable, which means that they are clumped by serums of all groups including serum of group AB, which normally lacks isoagglutinins, and even by the serum of the same individual. According to Thomsen, this irregular form of isoagglutination is due to a change in the red blood cells through which a latent agglutinogen becomes manifest and which reacts with an agglutinin normally present in all serums. This source of error in blood grouping is serious because the change may be completed within eight hours after contamination if the blood is kept at room temperature and may occur even at ice box temperature, though after a longer interval. The contaminating bacteria capable of such action are probably fairly common. The surest way to avoid this source of error is to observe aseptic technic, to use only fresh cell suspensions and to keep them in the ice box when not in use.

The fifth and last group of irregular isoagglutinins have been described recently by Toharsky and me [19] as bacteriogenic hemagglutinins. We isolated from a contaminated typing serum a gram-positive bacterium identified as belonging to the large group of diphtheroids. The bacterium was designated as Corynebacterium hektoenii. It imparts to the serum and plasma new hemagglutinating properties and makes them panagglutinating in fairly high titers at 22 C. and 37 C. Not only the bacterium but also the filtrates of its cultures have the same transforming ability. In addition to the change in the serum, the bacterium and its cultures make red cells panagglutinable by serums of all groups, thus producing the previously mentioned so-called Thomsen panagglutination phenomenon. Bacteriogenic hemagglutinins are of interest as a source of error in blood typings and as a potential danger as a contaminant of stored serums and plasma. The danger is enhanced by the fact that the keeping of typing serum or of therapeutic serum and plasma in refrigerators does not prevent the growth of the responsible bacterium.

16. Landsteiner, Karl, and Witt, D. H.: Observations on Human Isoagglutinins, Proc. Soc. Exper. Biol. & Med. **21**: 389, 1924.

17. Wiener, A. S.: Hemolytic Transfusion Reactions: I. Diagnosis, with Special Reference to the Method of Differential Agglutination, Am. J. Clin. Path. **12**: 189 (April) 1942.

18. Friedenreich, V.: The Thomsen Hemagglutination Phenomenon, Copenhagen, Levin and Munksgaard, 1930.

19. Davidsohn, Israel, and Toharsky, B.: The Production of Bacteriogenic Hemagglutination, J. Infect. Dis. **67**: 25 (July-Aug.) 1940; Bacteriogenic Hemagglutination, J. Immunol. **43**: 213 (March) 1942.

In eliminating typing errors due to cold agglutinins, one is helped by the failure of most of them to react at 37 C., but this does not help one in recognizing bacteriogenic hemagglutinins because they react readily at body temperature. Here too the best way to eliminate the source of error is to type the serum as well as the red cells and to remember that typing of red cells is only half of the job. Serum with bacteriogenic hemagglutinins will clump red cells of group O, which are normally not agglutinated by any serum. When one has reason to suspect that bacteriogenic panagglutination has developed, the way to prove it is to test the cells with serum of the same individual or with serum of group AB known to be free of cold agglutinins and to type the serum of the unknown blood specimen with red cells of known groups.

Several bactericidal and bacteriostatic agents have been found which prevent development of bacteriogenic hemagglutination.

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ABSTRACT OF DISCUSSION

DR. PHILIP LEVINE, Newark, N. J.: Recent studies indicate that about 90 per cent of intragroup transfusion reactions following isoimmunization either by repeated transfusions or by fetal blood during pregnancy occur in Rh individuals. Unfortunately not all cases can be detected by the demonstration of anti Rh agglutinins. In many cases it must be assumed that the anti Rh antibody is fixed to the tissue cells of the reticuloendothelial system. To prevent intragroup transfusion accidents, all Rh patients should receive blood from Rh donors. Also the modified cross matching test, i. e. incubation of patient's serum and donor's cells at 37 C. for fifteen to thirty minutes, should be carried out. Whenever anti Rh agglutinins could be demonstrated, they frequently behave like warm agglutinins, in contrast to those which react best at 20 C. or lower temperature. Occasionally an Rh patient immunized by the Rh factor may have several atypical agglutinins, as demonstrated by varying specificities at different temperatures. In such cases the compatibility tests should be carried out at 37 C., while incompatibilities detectable at lower temperature are probably of less significance. Rarely, however, atypical agglutinins acting at low temperature may cause transfusion reactions. In my opinion these are apt to occur in patients immunized either by repeated transfusions or by the fetus, but by blood factors other than Rh. In these instances, as in the exceptional cases of Wiener and Peters, i. e. cold anti Rh agglutinins, one cannot be certain whether the demonstrable antibodies or tissue antibodies are responsible for the transfusion reactions. This view does not conflict with the claim of Landsteiner and Levine that the atypical agglutinins present in 3 per cent of all normal individuals probably do not cause transfusion reactions. In these instances the atypical agglutinins inactive at 37 C. are physiologic for these individuals, in contrast to the atypical immune agglutinins mentioned. An appeal can be made to abandon the nomenclature of the blood groups by numbers. The letters O, A, B and AB indicate the correct theory of two dominant factors A and B and the recessive property determining group O. In cases of disputed paternity, tests are carried out for the presence or absence of the factors A, B, M, N and, in the future, also Rh. The factors A and B may be of importance also in causing fetal death. Accordingly, a discussion of these applications can be intelligible only if the terminology by letters is employed.

DR. FREDERIC FELDMAN, Brooklyn: Had the patient with the anti O agglutinin received transfusions with O blood? Had the O acted as an antigen? Does the same apply to the case with anti M agglutinin?

DR. ISRAEL DAVIDSOHN, Chicago: The patient that I referred to did not belong to blood group O but to A_1. He had received several blood transfusions before, both of the same blood group and of group O, without any untoward reactions, when it was found in the course of a cross agglutination that his serum clumped cells of his own group and of group O. This observation confirms exactly what Dr. Levine was telling us. The irregular isoagglutinins a_1 and a_2 belong to the group of cold agglutinins. After repeated transfusions or possibly of some infection, irregular isoagglutinins may appear. I have observed that the rise occurs in the course of infections even without immunization by means of blood transfusions. It is not known whether these agglutinins are entirely new or whether their titer rises and they become detectable, having been previously below the threshold of detectability. A similar mechanism may have operated in the case of the anti M agglutinin. That child did not receive any transfusions before. It is not a familial case. Both parents were investigated and they did not have anti M agglutinins. The origin of these anti M agglutinins is unknown.

Clinical Notes, Suggestions and New Instruments

BERIBERI HEART IN A 4 MONTH OLD INFANT

(WITH FOUR YEAR FOLLOW-UP)

HENRY RASCOFF, M.D., BROOKLYN

Infantile beriberi has rarely been reported in the continental United States. Waring [1] in 1928 recorded the occurrence of this disease in a 2 month old child with findings of cardiac hypertrophy, loss of knee reflexes, hepatic enlargement and finally heart failure. A poor nutritional background was given as the etiologic factor. Other observers [2] have mentioned the possibility of beriberi being one of the causes of enlarged hearts in occidental infants.

The following report is of an infant that for two months had been on a limited diet of boiled human milk and subsequently developed an enlarged heart, which diminished in size with thiamine hydrochloride therapy.

REPORT OF CASE

R. S., a white boy, was born at the Beth El Hospital on Feb. 19, 1938, two weeks before term and of normal spontaneous delivery. The stay in the hospital was uneventful, and he was discharged on the tenth day weighing 2 ounces (55 Gm.) above the birth weight of 5 pounds (2.3 Kg.). Shortly after reaching home the infant began to vomit; the next day diarrhea set in. For the following three weeks various formulas of sweet and acid milks were given with but little success. The vomiting and diarrhea persisted in varying degree and on March 20 the child was hospitalized.

On admission the infant weighed 5 pounds 8 ounces (2.5 Kg.). It was somewhat malnourished and dehydrated, but the rest of the examination was not remarkable. Clysis and venoclysis of 5 per cent dextrose in isotonic solution of sodium chloride were given. When the vomiting and diarrhea were controlled, feeding by mouth was begun with gradually increasing amounts of dextrose water. This was supplemented by and finally replaced by protein milk to which had been added 5 per cent of a preparation of maltose and dextrin. However, when a sufficient amount of formula calculated to the child's needs was given, the stools once more became watery and frequent. Parenteral feeding was again resorted to, and in addition a transfusion of 75 cc. of citrated blood given. This time human milk was introduced as the food of choice. The infant seemed to tolerate this and was discharged on April 15 on a diet of human milk boiled for thirty minutes, 50 mg. of ascorbic acid and 3 drops of vitamin D_2 daily. The weight of the child at this time was 5 pounds 14 ounces (2.6 Kg.).

1. Waring, J. I.: Beriberi in Infants, Am. J. Dis. Child. **38**: 52 (July) 1929.

2. Abt, I. A.: The Child's Heart in Avitaminosis, Am. J. Dis. Child. **50**: 455 (Aug.) 1935. Kugel and Stoloff.[10] Hoobler.[7]

Shortly after reaching home, the infant developed an upper respiratory infection and for two weeks there were bouts of diarrhea, which were again controlled by the feeding of boiled milk. For the ensuing six weeks the child gained weight on this form of milk and made satisfactory progress.

At the age of 4 months the infant suddenly became dyspneic and cyanotic. The temperature was not elevated. Examination of the chest revealed that the breath sounds were exaggerated, but no rales or bronchial breathing was elicited. There were no abnormal reflexes, nor was there edema of the extremities or dependent parts. The weight at this time was 10 pounds 13 ounces (4.9 Kg.). X-ray examination of the long bones gave normal results.

Physical and roentgen examination of the heart revealed a general cardiac enlargement (fig. 1). The heart sounds were only fair in quality. The electrocardiographic tracing did not show any abnormalities in conduction or in the contour of the individual waves; only a slight tachycardia of sinus origin. As the result of consultation with Dr. Bela Schick and Dr. Leo M. Taran, it was felt that in view of the apparent vitamin B_1 deficient diet we might be dealing with a beriberi heart. Accordingly, the child's daily diet was supplemented with 6 mg. of thiamine hydrochloride. Within two weeks the cyanosis and dyspnea were gone. At the age of 6 months the child was able to tolerate a formula of whole cow's milk and maltose with dextrin, precooked cereal and a few simple vegetables. At the age of 18 months there was still x-ray evidence of cardiac enlargement. However, the child was developing satisfactorily. His weight at this time was 31 pounds (14 Kg.) and he was 32 inches (81 cm.) tall.

At the age of 4 years the child is in excellent physical condition, weighing 48 pounds (22 Kg.) and measuring 43 inches (109 cm.) in height. X-ray examination of the cardiac shadow reveals it to be within normal limits (fig. 2).

COMMENT

Fehily [3] reported from Hong Kong that infants fed milk of mothers suffering from B_1 avitaminosis showed signs of infantile beriberi. These signs were grouped as acute, subacute and chronic. The acute form was characterized by cyanosis, dyspnea, rapid pulse and often sudden death, the mortality rate being 93 per cent. Children dying from the acute form responded in short order to tiki-tiki (extract of rice husks). She noted too that the milk from beriberi mothers was not only deficient in thiamine but gave a "peroxidase negative" reaction.

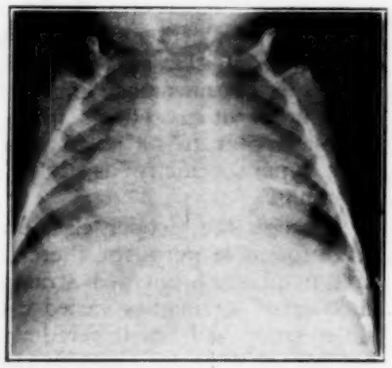

Fig. 1.—Generalized cardiac enlargement at the age of 4 months.

Peroxidase is an enzyme normally found in fresh milk and blood of mammals. It is destroyed by heat and is absent in certain conditions, as in the secreting milk of mothers suffering from beriberi. Its presence or absence is noted by the Arakawa reaction, which is based on the "oxidation of substances of a phenolic nature to colored compounds by a peroxide in the presence of a ferment peroxidase, which catalyzes the reaction." [5]

A "peroxidase negative" milk of mothers presenting signs of beriberi is an indication of B_1 avitaminosis, according to Fehily. Kendall [4] has shown that boiled human milk is low in thiamine content. These two features of milk from beriberi mothers, i. e. low thiamine hydrochloride content and "peroxidase negative" milk, were characteristic of the boiled human milk fed infant.[6] Another predisposing factor for the development of infantile beriberi in this child was the recurring prolonged diarrhea. It has been demonstrated that the poor utilization of food substances, such as in chronic diarrhea, plays a role in the etiology of this condition.[6]

The basis for the development of subclinical or clinical beriberi is often present in early infancy. The dietary of the average infant during the first three months of life is composed of human or cow's milk supplemented with carbohydrate, orange juice and some form of vitamins A and D. This diet is deficient in vitamin B_1.[7] When vomiting or diarrhea, both common in infancy, are present for any length of time the body is depleted of its vitamin reserve. In treating these gastrointestinal disturbances some form of boiled milk is usually given. Boiled milk, as previously noted, gives a peroxidase negative reaction and is low in thiamine hydrochloride. In view of this knowledge, the dietary of the average infant should be supplemented with 100 international units of vitamin B_1 daily. When diarrhea or vomiting is persistent, the amount given should be many times this dose.

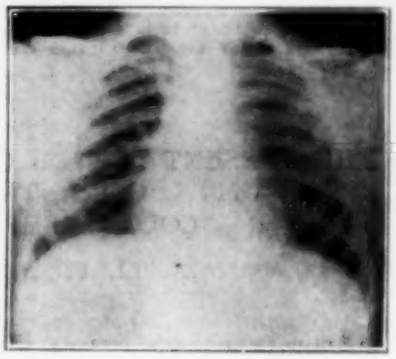

Fig. 2.—Normal configuration of the heart at the age of 4 years.

The group of heart conditions in infancy vaguely classified as idiopathic cardiac hypertrophy has been greatly reduced in recent years by the increased knowledge of the etiology and postmortem study of enlarged hearts in infancy. Scurvy,[8] rickets,[2] celiac disease [9] and congenital anomalies [10] have been found to be causative factors in this "idiopathic" condition. Infants suffering from cardiac enlargement of unknown origin should be given adequate doses of thiamine hydrochloride as a therapeutic test for beriberi heart.

One should also reexamine the sudden deaths attributed at present to status thymicolymphaticus. These may be the result of the acute form of beriberi; especially may this be true when a previous history reveals a diet deficient in vitamin B_1.

SUMMARY AND CONCLUSIONS

1. In a case of beriberi heart in a 4 month old infant the diagnosis was made clinically, and therapeutic response was noted with thiamine hydrochloride.

2. The daily diet of the average young infant is deficient in thiamine hydrochloride and should be supplemented with vitamin B_1. In cases of gastrointestinal disturbances the vitamin B_1 intake is to be increased.

3. Some cases at present diagnosed as idiopathic cardiac hypertrophy, or deaths attributed to status thymicolymphaticus, may be caused by infantile beriberi.

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3. Fehily, Lydia: J. Trop. Med. & Hyg. **44:** 21 (Feb. 15) 1941.
4. Kendall, Norman: J. Pediat. **20:** 65 (Jan.) 1942.
5. Dr. Irving Greenblatt of the chemistry laboratories of the Beth El Hospital found that several specimens of raw human milk which gave a positive peroxidase reaction on initial examination became peroxidase negative when subjected to heat of 78 C. for more than three minutes. Pasteurized milk gave a similar response, but evaporated milk was peroxidase negative without further heating.
6. Weiss, Soma: Occidental Beriberi with Cardiovascular Manifestations, J. A. M. A. **115:** 832 (Sept. 7) 1940.
7. Hoobler, B. R.: Symptomatology of Vitamin B Deficiency in Infants, J. A. M. A. **91:** 307 (Aug. 4) 1928.
8. Lehndorff, H., and Mautner, H.: Ergebn. d. inn. Med. u. Kinderh. **31:** 456, 1927.
9. Haas, S. V.: Arch. Pediat. **46:** 467 (Aug.) 1929.
10. Kugel, M. A., and Stoloff, E. G.: Dilatation and Hypertrophy of the Heart in Infants and in Young Children with Myocardial Degeneration and Fibrosis, Am. J. Dis. Child. **45:** 828 (April) 1933.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

MANY TYPES OF ANTIPNEUMOCOCCUS RABBIT SERUM HAVE APPEARED ON THE MARKET, AND THE MULTIPLICATION OF THESE TYPES HAS BEEN SO GREAT THAT THE COUNCIL VOTED TO SPONSOR A REPORT TO CLARIFY THE STATUS OF THESE SERUMS FOR THE TREATMENT OF HIGHER TYPES OF PNEUMOCOCCIC INFECTIONS. DR. MAXWELL FINLAND AGREED TO PREPARE A PAPER ON THIS SUBJECT AND ACCORDINGLY HAS PRESENTED THE FOLLOWING STATEMENT, WHICH THE COUNCIL HAS ADOPTED FOR PUBLICATION WITH APPRECIATION TO THE AUTHOR FOR THE EXTENSIVE WORK NECESSARILY ENTAILED IN THIS STUDY.

AUSTIN E. SMITH, M.D., Secretary,
COUNCIL ON PHARMACY AND CHEMISTRY.

THE PRESENT STATUS OF THE HIGHER TYPES OF ANTIPNEUMOCOCCUS SERUMS

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Antipneumococcus serums from rabbits have now been accepted by the Council for types I, II, III, IV, V, VII, VIII and XIV.[1] An evaluation of the other types of antipneumococcus serums, which for convenience will be called the "higher types,"[2] involves a consideration of the following problems: (1) the present status of the pneumococcus types, particularly as it concerns serologically related types; (2) the relation of the higher types to disease in general and to pneumonia in particular; (3) the efficacy of antipneumococcus rabbit serums in the treatment of the pneumonias associated with pneumococci of these types; (4) the status of specific antiserum therapy for pneumonia in relation to the use of effective sulfonamide compounds (*a*) as a supplement or (*b*) as a substitute for the drugs, and (5) the use of serums in the treatment of focal pneumococcic infections, particularly meningitis and peritonitis.

It may be stated at the very outset that, from the point of view of adequate, cleancut and conclusive data which will withstand analysis by statisticians or by intelligent critics or skeptics, no solution to these problems can be expected at the present time. Nor is it likely that proper data will be forthcoming in the near future that will be any more helpful. Nevertheless it seems advisable to review briefly the available facts and to try to arrive at some intelligent attitude and practical approach to the problem of the use of the higher type antipneumococcus rabbit serums.

PRESENT STATUS OF THE CLASSIFICATION OF PNEUMOCOCCI INTO TYPES

In 1932 Cooper and her co-workers[3] separated the unclassified strains of pneumococci, which had previously been included in group IV, into twenty-nine new types designated as types IV to XXXII. Only a small percentage of strains that they had isolated in New York City did not fall within these types. A few cross reactions were noted, particularly between types II and V, III and VIII, VII and XVIII and XV and XXX. Type XXVI was found to react with the original type VI to such an extent that the former was designated VIb and the latter VIa. Strains of these types have since been included under the single designation type VI by most workers. The original type XXX is also usually eliminated because of the difficulty in differentiating it from type XV. With these two changes, the Cooper classification has been adopted and used for clinical and epidemiologic purposes throughout the world.

Pneumococci of almost all these types have been found wherever sufficient numbers of strains from different sources have been studied. The percentage distribution of these types in various pathologic conditions and in normal individuals has varied in different localities, and at different times in the same place. The percentage of untyped strains which failed to react with antiserums for the Cooper types likewise varied considerably. In South Africa, where a separate and equally extensive classification had been in use, it was found that only two of the Cooper types did not have counterparts in the local types and, conversely, only two of the South African types were not represented in the Cooper classification, which has since been adopted there.[4]

The various pneumococcus types are generally considered to be quite stable. Transformation of one type to another has been accomplished both in vitro and in experimental animals.[5] To do this, however, it has been necessary first to convert the original type specific pneumococcus by special procedures from the so-called smooth and virulent (and presumably pathogenic) form to the avirulent and non-type specific rough variant. The latter is then grown, either in vitro or in the peritoneal cavity of a mouse, in the presence of smooth killed organisms of the type to which it is to be converted. The type specific polysaccharide may be used in place of the killed organisms for this purpose. It is not known whether similar transmutations take place in nature, but it seems highly improbable. In general, type specific pneumococci obtained from the nasopharynx or other sources in the absence of manifest disease appear to be about as stable with respect to their type specificity as those obtained from active infections.

Although the Cooper classification has proved adequate for most purposes, there still remained a significant number of untyped strains. The proportion of unclassified strains has varied with the type of material under study and has differed widely in various localities and at different times in the same region or even in the same laboratory. As interest in the use of antipneumococcus serums increased (before effective sulfonamide drugs became available) various investigators became concerned over the diagnostic and therapeutic difficulties involved in the management of individual sick patients or groups of cases. New types were discovered when inordinate numbers of untyped strains

From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School.

1. Antipneumococcic Serums, Council on Pharmacy and Chemistry, J. A. M. A. **115:** 460-461 (Aug. 10) 1940; **116:** 2597 (June 7), **117:** 1264 (Oct. 11), 1707 (Nov. 15) 1941. Antipneumococcic Serum (Rabbit) Type XIV, ibid. **117:** 2073 (Dec. 13) 1941.

2. All types other than I, II and III have usually been included in the "higher types." Since the present discussion is limited mostly to those types for which antiserums are not yet accepted by the Council, it seems appropriate and convenient for the purpose at hand to exclude all of the "accepted" types from the category of "higher types."

3. Cooper, Georgia; Rosenstein, Carolyn; Walter, Annabel, and Peizer, Lenore: The Further Separation of Types Among the Pneumococci Hitherto Included in Group IV and the Development of Therapeutic Antisera for These Types, J. Exper. Med. **55:** 531-554 (April) 1932.

4. Ordman, David: Pneumococcus Types in South Africa: A Study of Their Occurrence and Distribution in the Population and the Effect Thereon of Prophylactic Inoculation, Pub. South. African Inst. M. Res. **19:** 1-27 (April) 1938.

5. Neufeld, F., and Levinthal, W.: Beitrage zur Variabilität der Pneumokokken, Ztschr. f. Immunitätsforsch. u. exper. Therap. **55:** 324, 1928. Griffith, F.: Significance of Pneumococcus Types, J. Hyg. **27:** 113-159 (Jan.) 1928. Dawson, M. H.: Interconvertibility of R and S Forms of Pneumococcus, J. Exper. Med. **47:** 577 (April) 1928.

from patients with severe pneumonia or meningitis were encountered in rapid succession. For example, at the State Serum Institute in Copenhagen, diagnostic serums were prepared against two hitherto unknown strains. In the course of half a year one of these types was demonstrated in 31 patients, including 2 with meningitis, and in 9 normal individuals; the second type was found in 72 patients and in 10 normal individuals.[6]

In addition, as therapeutic serums for some of the types were used, some clinicians were struck with the fact that certain patients failed to show a beneficial response to what seemed to be adequate doses of antiserum. Investigations in some of these cases revealed that the failures were due to the fact that the causative organism was a pneumococcus which was serologically related to but not identical with the strain used in producing the therapeutic antiserum. Better results were obtained when specific serum for the newly discovered type was used.[7] Other types were discovered because of cross reactions in horse or rabbit diagnostic serums.[8] Such cross reactions were particularly frequent in agglutination reactions with horse serums, but they were also noted when the Neufeld capsular swelling reaction with diagnostic rabbit serums was used for typing. These facts led to a continued interest in the classification of pneumococci, which resulted in the recognition of many entirely new types and a number of types closely related to those previously classified.

In 1940 Kauffmann, Mørch and Schmith[9] at the Danish State Serum Institute determined serologically twenty new types of pneumococci in addition to the thirty Cooper types. They worked out the antigenic components of ten groups, each of which consisted of from two to four serologically related types, and indicated which serums were necessary to establish the specific type diagnosis. The importance of having type specific antibodies for therapy has already been mentioned. In discussing the significance of their new types for diagnosis and treatment the Danish workers suggested that, for practical purposes, polyvalent serums could be prepared for the related types. Bjoerneboe[10] of the same laboratory showed that equally high titers of antibody could be obtained for each of the related types in this manner. He demonstrated it clearly for type VII and its three related types, for example. It is not known, however, whether the efficacy in human therapy in this respect parallels the mouse protective or other antibody titers. If this is assumed to be the case, then the practitioner need not be burdened with the intricacies of the many related types. He would then be concerned in diagnosis only with the main group or type and would obtain a therapeutic serum which would include antibodies for all the known related types.

Walter and her associates[11] of the Bureau of Laboratories of the New York City Department of Health described seventeen new types of pneumococci, of which nine were distinct from types I to XXXII and eight showed definite cross reactions with other types and were therefore called subtypes. These types were correlated with those of other workers and a terminology was recommended which included their own new types and those of Kauffmann. The original type XXVI of Cooper was officially omitted and types VIa and VIb were considered identical and the letters omitted. The original type XXX was included as type XVa and a new strain was designated as type XXX. Including one new type and six new subtypes of Kauffmann's, Walter's classification comprised a total of forty distinct types and fifteen subtypes.

Mørch[12] continued the work at the Copenhagen laboratory and subsequently presented eighteen additional types. He correlated his types with those of Walter and Kauffmann and their respective co-workers and extended the latters' schema for the diagnosis of related types on the basis of the capsular antigenic components. He also presented a method of preparing serums for determining and controlling the titer of each of these components. This study raised the total number of pneumococcus types to sixty-eight, of which forty-one are distinct types numbered I to XLII (excluding XXVI). The remaining twenty-seven types are included in fourteen groups, each consisting of from two to four related types. Mørch again pointed out the importance of having antibodies against all the antigenic components in therapeutic antiserums. He also emphasized the practicability and advisability of using mixed vaccines composed of pneumococci belonging to a group of related types in the immunization of animals for this purpose. Epidemiologically, however, the individual types within the groups of related types may each become significant under special circumstances.

In their most recent report to the American Public Health Association, the Standard Methods Committee[13] was of the opinion that the classification of pneumococcus types should be not only scientifically correct but, if possible, should be readily understood and applicable to the epidemiologic and clinical purposes for which pneumococcus typing is most generally employed. Conceivably, at least some of the types are not of sufficient importance to warrant their inclusion in routine public health and hospital practice. Should this prove to be true, they indicated that an abbreviated routine might prove desirable.

SIGNIFICANCE OF THE HIGHER TYPES OF PNEUMOCOCCI IN DISEASE

The work on the separation of types among the pneumococci has had as its ultimate or most important objective either the possibility of preparing effective specific antiserums for the treatment of patients or, as in the South African work, the development of vaccines for the prevention of pneumococcic infections. Therapeutic antiserums were prepared in the early work

6. Vammen, B.: Serological Variants of Pneumococcus Types 9 and 10, J. Immunol. **37:** 359-365 (Oct.) 1939.

7. Davidson, Arnold, and Bullowa, J. G. M.: Occurrence, Clinical Characteristics and Therapy of Pneumococcus XXXIII Pneumonia, J. Infect. Dis **66:** 178-180 (March-April) 1940.

8. Walter, Annabel W.; Blount, Katharine D.; Beattie, Marian W., and Colter, Hannah Y.: A Distinct Type of Pneumococcus Immunologically Related to Type 9 (Cooper), J. Infect. Dis. **66:** 181-183 (March-April) 1940. Welch, Henry; Borman, E. K., and Mickle, F. L.: Preparation and Analysis of Diagnostic Antipneumococcus Serum, Am. J. Pub. Health **29:** 35-42 (Jan.) 1939. Forster, G. F., and Shaughnessy, H. J.: Occurrence of Strains of Pneumococci Which React with More Than One Type Specific Antipneumococcus Serum, Proc. Soc. Exper. Biol. & Med. **44:** 306-309 (May) 1940. Finland and Brown.[38] Vammen.[6] Davidson and Bullowa.[7]

9. Kauffmann, F.; Mørch, E., and Schmith, K.: On the Serology of the Pneumococcus Group, J. Immunol. **39:** 397-426 (Nov.) 1940.

10. Bjoerneboe, M.: Ueber die Schützwirkung verschiedener Antistoffkomponenten in Type 7 Pneumokokkenseren, Ztschr. f. Immunitätsforsch. u. exper. Therap. **99:** 160-167, 1940; Serum Protein and Antistoffprotein bei Immunisierung mit mehreren Antigenen, ibid. **99:** 245-256 (Jan. 15) 1941.

11. Walter, Annabel W.; Guevin, Virginia H.; Beattie, Marian W.; Colter, Hannah Y., and Bucca, Helen B.: Extension of the Separation of Types Among the Pneumococci: Description of Seventeen Types in Addition to Types 1-32 (Cooper), with Recommendations for Terminology of All Types Reported Through 1940, J. Immunol. **41:** 279-294 (July) 1941.

12. Mørch, E.: Further Studies on the Serology of the Pneumococcus Group, ibid. **43:** 177-202 (Feb.) 1942.

13. Robinson, E. S.; Defries, R. D.; Muckenfuss, R., and Veldee, M. V.: Report of Standard Methods Committee. Biological Products. Types of Pneumococci, Am. Pub. Health Assoc. Year Book, 1941-1942, Am. J. Pub. Health **32:** suppl., p. 152 (March) 1942.

at the New York City Laboratories almost as soon as the new types were established and shown to be fairly prevalent.[14] The necessity of using horses for immunization limited this phase of the work considerably. Further diagnostic and therapeutic serums were then prepared with strains from severely ill patients which failed to agglutinate or showed atypical reactions with antiserums for available types.[3] In the accounts given by Cooper and Walter and their co-workers[15] the sources of the strains used in establishing the new types are given. Each of the new types included some strains isolated from blood cultures or autopsy material of patients with pneumonia, or from spinal fluid of patients with meningitis.

As already mentioned, the more recent types resulted from work undertaken because of diagnostic and therapeutic difficulties in severely ill patients. The use of rabbit serums, both in diagnosis and in treatment, made possible a more rapid extension of the work than was feasible when horses were employed for the preparation of antiserums. Some of the new types were soon shown to be quite prevalent, as evidenced by the first two types isolated at the Danish Serum Institute.[6] A new strain identified in our laboratory[16] and later called type XIa[11] was found at the Boston City Hospital in more than 25 cases in one season. The new type XXXIII, which gives cross reactions with type IX antiserums, was identified at about the same time in New York City[17] and in Copenhagen[6] and was also isolated by us from patients with pneumonia, meningitis and peritonitis who failed to show a favorable response to treatment with type IX therapeutic antiserum. In the New York City laboratory during the first five months of 1940, among 2,591 specimens from patients with pneumonia, the two new types XXXIII and XXXV were found forty-five and seventy-one times respectively, and the two new subtypes Xa and XIa were found thirty-three times and fifty times respectively. These four new types each occurred more frequently than any of twelve different types among those included in the Cooper classification.[18] Except for type XXXIII, however, very little additional data concerning the new types are available, and there is almost no information about the efficacy of therapeutic antiserums in the treatment of pneumonia due to these new types or subtypes. The rest of the discussion will therefore be concerned primarily with the original Cooper types.

In cases of pneumonia the etiologic role of any pneumococcus that is recovered is not always simple to determine, particularly if the only source of that organism is the sputum or a throat culture. Under such conditions a knowledge of the relative frequency with which various types of pneumococci are found in lobar or atypical pneumonias, in certain focal infections and in the nose and throat of normal persons is of some help. In patients with pneumonia, the relative frequency with which the different types of pneumococci are found in blood cultures, in cultures obtained from the lung during life or at autopsy or in purulent focal complications, and the development of specific antibodies during recovery for types found in the sputum aid in assessing their etiologic significance. A brief review of some of the available data concerning a few of these points, particularly in relation to the "higher" types of pneumococci, is therefore pertinent.

All of the types from I to XXXII have been found with varying frequency in cases of pneumonia, in a variety of focal infections and in normal persons without apparent disease.[19] Types IV, V, VII and VIII are usually the most frequent of the Cooper types found in cases of typical lobar pneumonia. In atypical or bronchopneumonias the distribution of types is more like that found in normal persons.[20] In the pneumonias complicating pregnancy and the puerperium, the incidence of pneumococcus types is essentially the same as in cases of primary lobar pneumonia,[21] while in those complicating operations and trauma the type distribution is intermediate between that found in normal persons and that found in patients with lobar pneumonia.[22] In the pneumonias of infants and children, type XIV predominates and types VI and XIX are frequent.[23] The latter types are also very frequent in normal persons.[24]

Multiple types of pneumococci are often found in sputum and sometimes from other sources in patients with pneumonia.[25] This is particularly true of infants and children and has been recognized more readily since the introduction of the Neufeld method of direct typing. These multiple types (or the finding of a pneumococcus and some other organism) may represent either a true simultaneous infection or consecutive infections or, most commonly, one of the types is etiologic and the other is a normal inhabitant of the respiratory tract and not involved in the infection.[26] Some types, when found under such conditions, almost always prove to be etiologic, others only rarely prove to be related to the disease, while still others occupy an intermediate position.

Bullowa[27] listed 225 strains obtained from adult cases of pneumonia with multiple infections. He classified these strains into those which occurred as definite pathogens, i. e. in blood cultures, chest pus or lung suction, and those which were indeterminate or possibly nonpathogenic and were obtained only from sputum. There were 114 strains in the former and 211 in the latter. Among the pathogenic strains, 92 were of the "accepted" types I to VIII (excluding VI) or XIV, while 22, or 10.5 per cent, were "higher" types. Among the possible nonpathogens, 52 per cent were of "higher" types. Of the 193 strains of "Council accepted" types, 48 per cent were definite pathogens, while of the 132

14. Cooper, Georgia; Edwards, M., and Rosenstein, Carolyn: The Separation of Types Among the Pneumococci Hitherto Called Group IV and the Development of Therapeutic Antiserums for These Types, J. Exper. Med. **49**: 461-474 (March) 1929.

15. Cooper, Rosenstein, Walter and Pilzer.[3] Walter, Guevin, Beattie, Colter and Bucca.[11] Cooper, Edwards and Rosenstein.[14]

16. Finland, Maxwell, and Brown, J. W.: A Study of Strains of Pneumococci Immunologically Closely Related to Both Type XI and Type XVI Pneumococci, J. Immunol. **35**: 141-153 (Aug.) 1938.

17. Davidson and Bullowa.[7] Walter, Blount, Beattie and Colter.[9]

18. Walter, Guevin, Beattie, Colter and Bucca.[11] Cooper, Rosenstein, Walter and Peizer.[3]

19. Sulkin, S. E.: The St. Louis Pneumonia Control Program: Epidemiological Aspects, J. Missouri M. A. **37**: 435-440 (Oct.) 1940. Ordman.[4] Bullowa.[27] Finland.[20] Straker, Hill and Lovell.[24]

20. Finland, Maxwell: The Significance of Specific Pneumococcus Types in Disease, Including Types IV to XXXII (Cooper), Ann. Int. Med. **10**: 1531-1542 (April) 1937.

21. Finland, Maxwell, and Dublin, T. D.: Pneumococcic Pneumonias Complicating Pregnancy and the Puerperium, J. A. M. A. **112**: 1027-1032 (March 18) 1939.

22. Stoneburner, L. T., III, and Finland, Maxwell: Pneumococcic Pneumonia Complicating Operations and Trauma: Analysis of Two Hundred and Seventy-Nine Cases of Postoperative and Ninety-Two Cases of Post-Traumatic Pneumonia Associated with Typed Pneumococci, J. A. M. A. **116**: 1497-1504 (April 5) 1941.

23. Nemir, Rose L.; Andrews, Elizabeth T., and Vinograd, Julia: Pneumonia in Infants and Children: A Bacteriologic Study with Special Reference to Clinical Significance, Am. J. Dis. Child. **51**: 1277-1295 (June) 1936. Bullowa, J. G. M., and Greenbaum, Evelyn: Pneumococcic Pneumonia in Infants and in Children, ibid. **53**: 22-31 (Jan.) 1937. Bullowa.[27] Andrews.[25]

24. Straker, Hill and Lovell.[20] Sulkin.[19]

25. Bullowa.[27] Andrews.[25] Nemir, Andrews and Vinograd.[23]

26. Finland, Maxwell: The Significance of Mixed Infections in Pneumococcic Pneumonia, J. A. M. A. **103**: 1681-1686 (Dec. 1) 1934.

27. Bullowa, J. G. M.: The Management of the Pneumonias, New York, Oxford University Press, 1937.

"higher" type strains only 16.7 per cent were obtained from blood culture, pleural fluid or lung suction.

Andrews [28] divided the pneumococcus types found in the pneumonias of infants and children into three etiologic groups. In group A, she included types I, V, XIV and XXII and the less frequent types II, VII, X, XII and XVII. These types appeared to be causative in all patients with lobar pneumonia from whom they were recovered; they were associated with a high incidence of pneumonia in infected persons, a high mortality among infants and a pronounced tendency to disseminate among the members of the families of patients with these types and a relatively higher incidence in the families of patients with pneumonias due to other types or in families in which there were no cases of pneumonia. Finally, group C included the least active types III, VIII, XIII, XV, XVI, XIX, XX and XXVIII. These types appeared to be responsible for lobar pneumonia in very few patients in whom they were found, evidence for familial dissemination was uncommon and they were most often recovered from persons who were in contact with heterologous types. Differences in incidence of types, in the relation to lobar pneumonia and in their dissemination within family groups was also found to vary with age.

TABLE 1.—*Relation of "Higher" Types of Pneumococci to Pneumonia and Other Infections as Indicated by the Relative Frequency of Their Occurrence as Compared with the Types for Which Therapeutic Serums Have Been Accepted by the Council*

			"Accepted" Types (I, II, III, IV, V, VII, VIII, XIV)		"Higher" Types (Remaining Types of Cooper [5])		
Source of Cases	Sources of Pneumococci	Number of Cases	Per Cent Incidence	Per Cent Mortality	Per Cent Incidence	Per Cent Mortality	Comment
New York State,[29] Illinois [30] and Pennsylvania [31]	All "typed" pneumococcic pneumonias	29,172	78.5	11.8	21.5	10.5	All Cooper types and XXXIII represented
	Fatal cases only	3,355	80.4		19.6		
Harlem,[32] Bellevue [33] and Boston City Hospital [34]	All "typed" pneumococcic pneumonias (adults):	12,049	74.8	22.3	25.2	24.2	All Cooper types and XXXIII represented among the fatal and the bacteremic cases
	Fatal cases	2,762	73.4		26.6		
	Positive blood cultures	2,516	86.8 (Positive blood cultures in 24.2 per cent)	59.3	13.2 (Positive blood cultures in 10.9 per cent)	67.4	
Harlem Hospital (Bullowa [27])	Adult pneumonias; "lung suction"	1,477	34.7		4.6		No pneumococci from remaining cases; 7 of the "higher" types not represented
Boston City Hospital (Finland [29])	"Typed" pneumococcic pneumonias in adults:	2,848	76.4	41.5	23.6	35.9	2,172 cases were of "accepted" types; of these 15.3% were "secondary," 14.5% were atypical pneumonias; 676 cases were of "higher" types; of these 43.8% were "secondary," 45.1% were atypical pneumonias
	Lobar pneumonias	2,229	83.4	37.8	16.6	27.5	
	Atypical (broncho-) pneumonias	619	50.7	63.0	49.3	46.2	
	"Primary" pneumonias	2,228	81.7	35.7	19.3	23.0	
	"Secondary" pneumonias	620	61.3	69.5	39.7	58.6	
	Cases with autopsy	684	76.6		23.9		524 cases at autopsy were of "accepted" types; of these 30.9% were atypical pneumonias; 160 cases at autopsy were of "higher" types; of these 80.0% were atypical pneumonias
	Lobar pneumonias	394	91.9		8.1		
	Atypical pneumonias	290	55.9		44.1		
	Focal infections without pneumonia	243	74.5		25.5		
Five hospital series [26]	"Typed" pneumonias in infants and children	2,506	54.9		45.1		All Cooper types and XXXIII represented
South African (Ordman [4])	Pneumococcic pneumonias	1,496	60.6		10.8		Remaining cases were of "native" types not represented in the Cooper classification; three Cooper types were not represented
	Inoculated cases	447	45.6		14.6		
	Uninoculated cases	1,049	67.1		9.2		
Collected cases (Hollander [37])	"Typed" pneumococcic meningitis	189	56.7		43.3		Excluding 71 cases of "types not stated" and 4 cases of type "over XXXII"
England [38] and Germany [39]	Pharyngeal cultures of healthy pneumococcus carriers	3,543	30.1		53.2		16.7% were negative I - XXXII; of the 30.1% "accepted" types almost half (14.9%) were type III

A similar attempt to classify the types with respect to pneumonia in adults would result in a considerably different alinement. For example, type IV would belong in group A, types III, VIII and XIV might well fit into group B and type VI would be in group C. There would undoubtedly be considerable variations, depending on the source of the material for such a classification and the kind of data available for evaluating the etiologic relationships. One would also expect appreciable differences in different localities and even at different times in the same region.

In table 1 is listed a group of miscellaneous pertinent data collected from various sources for the purpose of bringing out the relative frequency and significance

28. Andrews, Elizabeth T.: Lobar Pneumonia in Children: Differentiation of Recovered Pneumococci into Etiologic Groups and Their Familial Distribution, Am. J. Dis. Child. **54**: 1285-1310 (Dec.) 1937.

of the "Council accepted" types, I, II, III, IV, V, VII, VIII and XIV, and the other or "higher" types of the Cooper classification. In a large series of "typed" pneumococcic pneumonias collected by the pneumonia control divisions of the departments of health of three large states (New York,[29] Illinois [30] and Pennsylvania [31]) the higher types accounted for 21.5 per cent of the cases. In another large series of such cases in adults from three municipal hospitals in New York and Boston (Harlem,[32] Bellevue [33] and Boston City Hospital [34]), 25.2 per cent were associated with higher type pneumococci. In both of these series types XV and XVI, and all of the types numbered beyond XX, each accounted for less than 1 per cent of the total of "typed" cases. Types X, XII and XIII each occurred in less than 1 per cent of the "state" cases but were each found in more than 1 per cent of the hospital cases.

The mortality in all the cases of the "higher" types was about the same as in the cases of the "Council accepted" types of each of these two series. This seems surprising, since the higher types are usually considered to be "less virulent" and presumably less fatal. The following evidence lends support to such a belief: 1. Most of the higher types are definitely less virulent for mice.[35] 2. Positive blood cultures are less frequent in cases with pneumococci of the higher types and, likewise, higher types are relatively less frequent in bacteremic cases of pneumococcic pneumonia. 3. Higher types were relatively infrequent in cultures obtained directly from the pneumonic lung during life; in fact, seven of the higher types were not encountered in lung cultures from 1,477 cases.[27]

A likely explanation of this paradox is found in the analysis of a series of cases from the Boston City Hospital, also shown in table 1. The proportion of these cases that were due to the higher types was about the same for the entire series and for the cases that came to autopsy and was similar, in turn, to that found in the two larger series already mentioned. The mortality in all the cases of the higher types was only slightly less than in the other cases and not considerably lower, presumably because of the following combination of circumstances: 1. There was an appreciably lower incidence of higher types among the typical cases of lobar pneumonia and a relatively much greater proportion of these types in the atypical pneumonias. 2. There was a relatively lower incidence of higher types in the primary pneumonias and a much greater incidence among the "secondary" pneumonias, i. e. among the pneumonias complicating other serious illnesses. 3. The mortality was significantly lower in the pneumonias of the higher types, as compared with that of the "accepted" types, in all groups of cases; that is, in the lobar and the atypical pneumonias and in the primary and the secondary pneumonias. 4. The mortality in all the atypical pneumonias and in all the secondary pneumonias, however, was considerably higher than in the lobar and in the primary pneumonias, respectively, regardless of the pneumococcus types. 5. Also secondary and atypical pneumonias were about three times as frequent among the cases of the "higher" types as among those of the "accepted" types. It would thus appear that factors, presumably in the host, which predispose to the occurrence of secondary or atypical pneumonias are also responsible for the high mortality in the cases of the higher types in spite of the lesser virulence and invasiveness of these organisms.

In the pneumonias of infants and children [36] the higher types are about twice as frequent as in the pneumonias of adults. As already noted, types XIV, VI and XIX are particularly frequent in infants and children but are relatively infrequent in adults.

The South African cases listed in table 1 show the probable effect of prophylactic vaccination. The vaccines used were prepared from prevalent types of pneumococci and presumably contained few, if any, of the "higher" types. The incidence of the latter among the inoculated patients was appreciably higher than among the uninoculated patients. Contrariwise, the "accepted" types, at least some of which were included in the vaccines, were definitely less frequent in the inoculated patients.

The "higher" types accounted for about one fourth of the Boston City Hospital cases of purulent pneumococcic infections in patients without pneumonia. In Hollander's [37] collected series 43.3 per cent of 189 typed cases of pneumococcic meningitis were of the higher types. In our experience the latter types are relatively more frequent in cases of meningitis in the absence of pneumonia than when the meningitis occurs as a complication of a pulmonary infection.

Among healthy pneumococcus carriers, more than half of the strains of pneumococci identified by two groups of investigators were of the "higher" types, about 30 per cent were of the "accepted" types and approximately one sixth did not correspond to any of the Cooper types. All the Cooper types, however, were represented in each of the two groups of carriers. The distribution of individual types varied in the individual reports, although not widely, considering the numbers of cases and types and the many other factors involved. There were some striking discrepancies, however, as, for instance, in the case of type XVIII. This type

29. Data for New York State, excluding New York City, are from the Bureau of Pneumonia Control of the New York State Department of Health. They were furnished to the author in personal communications from Drs. Edward D. Rogers and Anne M. Bahlke.

30. Rosi, Reno; Sagen, O. K., and Prange, E. A.: Pneumonia in Illinois, 1938-1941, J. A. M. A. **119:** 1011-1015 (July 25) 1942. These data were furnished to the author prior to publication in personal communications from Drs. Harry A. Lindberg, Reno Rosi and O. H. Robertson.

31. Faller, C. P.; Quickel, K. E., and Smith, C. W.: A Statistical Study of 5,977 Cases of Pneumonia, with Mortality Statistics of 9,162 Serum and Sulfapyridine Treated Cases Collected from Recent Literature, Pennsylvania M. J. **43:** 789-806 (March) 1940. Stahle, D. C.: A Clinical Analysis of Fifteen Thousand Cases of Pneumonia: An Evaluation of Various Therapeutic Agents, J. A. M. A. **118:** 440-446 (Feb. 7) 1942. Dr. Stahle also provided further details concerning the individual higher types in personal communications.

32. Data furnished in a personal communication from Dr. Bullowa. Bullowa.[27]

33. Plummer, Norman, and others: Chemotherapy versus Combined Chemotherapy and Serum in the Treatment of Pneumonia: A Study of 607 Alternated Cases, J. A. M. A. **116:** 2366-2371 (May 24) 1941.

34. Tilghman, R. C., and Finland, Maxwell: Clinical Significance of Bacteremia in Pneumococcic Pneumonia, Arch. Int. Med. **59:** 602-619 (April) 1937. Finland, Maxwell; Spring, W. C., Jr., and Lowell, F. C.: Specific Treatment of the Pneumococcic Pneumonias: An Analysis of the Results of Serum Therapy and Chemotherapy at the Boston City Hospital from July 1938 Through June 1939, Ann. Int. Med. **13:** 1567-1593 (March) 1940. Finland, Maxwell; Lowell, F. C., and Strauss, Elias: Treatment of Pneumococcic Pneumonias with Sulfapyridine, Sulfathiazole and Serum: Analysis of the Results of Specific Therapy at the Boston City Hospital from July 1939 Through June 1940, ibid. **14:** 1184-1198 (Jan.) 1941.

35. Cooper, Rosenstein, Walter and Peizer.[3]

36. Greengard, Joseph; Raycraft, W. B., and Motel, W. G.: Effect of Chemotherapy on Pneumonia in Infants Under One Year of Age, Am. J. Dis. Child. **62:** 730-742 (Oct.) 1941. Christian, H. S.; Jorgensen, G. M., and Ellis, Catherine: Treatment of Pneumococcic Infections in Children with Sulfapyridine, ibid. **59:** 1-18 (Jan.) 1940. Butler, C. D., and others: Pneumonia in Children: A Review of Seven Hundred and Thirty-One Cases, J. A. M. A. **117:** 1840-1843 (Nov. 29) 1941. Bullowa.[27] Nemir, Andrews and Vinograd.[23]

37. Hollander, G.: The Prognosis of Pneumococcic Meningitis Treated with Chemotherapy, Am. J. M. Sc. **203:** 370-376 (March) 1942.

accounted for less than 1 per cent of the normal carrier strains of pneumococci in the English series [38] and 13.8 per cent of those in Gundel's [39] comparable studies.

The distribution of the individual types in five different groups of cases is shown in table 2. All the Cooper types are represented in each of the pneumonia groups and in the normal carriers,[40] but their incidence varied widely. Except for a few discrepancies, the distribution of types in cases of pneumonia was very similar in the state [41] series and in the adult hospital cases,[42] but the mortalities in the various types are consistently higher in the latter. This may be due chiefly to the fact that a large percentage of the cases in the hospital series occurred before the introduction of effective sulfonamides, while almost all of the "state" cases occurred after 1938. The hospital cases, however, also represent a much more severe group of infections.

The incidence of positive blood cultures in the adult hospital cases of the various types is also shown in table 2. This gives one an opportunity to compare the mortality of the individual types with their "invasiveness," the incidence of bacteremia being a good index of the latter. The types seem to fall roughly into three groups according to the incidence of bacteremia. The first group includes all the "accepted" types and, in addition, types XII and XXV. These may be considered the most invasive types; in more than one sixth of the cases of each of these types (17.4 to 38.7 per cent) the blood cultures are positive. In this group the mortality percentage was roughly about the same as the incidence of bacteremia. In the case of types I, II and V the relatively lower mortality rate may be explained in part by the use of effective serums in a large proportion of cases. The second group includes types IX, X, XVIII, XIX, XX, XXII, XXIII and XXIV, which were intermediate in their invasiveness. Between 8.6 and 14.5 per cent of the cases in each of these types presented positive blood cultures. The percentage of mortality in each of these types was roughly twice as high as the incidence of bacteremia. The third group includes the remaining "higher" types, which were the least invasive. With two exceptions the percentage of mortality in each of these types was from three to six times as great as the percentage of positive blood cultures.

This classification obviously cannot be considered to be a rigid one. Some of the types are obviously borderline and might be found to fall into different groups if more data were available. Furthermore, the same types may behave differently under special circumstances. From the point of view of specific serum therapy of pneumonia, however, such a classification may be of help. If such serums are of value, then it is presumably in the "invasive" types that they should have their greatest use.

TABLE 2.—*Distribution of Pneumococcus Types in Pneumonia and in Healthy Carriers, with Mortality Rates and Incidence of Bacteremia, by Types, in Selected Groups of Cases of Pneumonia*

	Pneumonias of 3 Large States [41]				Pneumonias of Adults in 3 Municipal Hospitals [42]						Pneumonias in Infants and Children [40]		Healthy Carriers [40]	
									Bacteremic Cases					
Pneumococcus Type	Number of Cases	Per Cent of Total	Died	Per Cent Mortality	Number of Cases	Per Cent of Total	Died	Per Cent Mortality	Number	Per Cent of Type	Number	Per Cent of Total	Number	Per Cent of Total
I	9,554	32.8	1,062	11.1	2,573	21.4	451	17.5	655	25.4	384	15.3	42	1.2
II	3,128	10.7	422	13.5	888	7.4	276	31.1	344	38.7	59	2.4	36	1.0
III	2,978	10.2	507	17.0	1,480	12.3	536	36.2	356	24.0	103	4.1	529	14.9
IV	1,038	3.6	122	11.8	643	5.3	136	21.2	123	19.1	122	4.9	233	6.6
V	1,325	4.5	132	10.0	809	6.7	148	18.4	198	24.5	134	5.3	12	0.3
VI	902	3.1	84	9.3	330	2.7	67	20.3	25	7.1	309	12.3	368	10.4
VII	2,192	7.5	189	8.7	1,116	9.3	189	16.9	194	17.4	99	4.0	71	2.0
VIII	1,940	6.7	206	10.6	990	8.2	164	16.6	205	20.7	40	1.6	134	3.8
IX	317	1.1	32	10.1	266	2.2	77	28.9	35	13.2	43	1.7	80	2.3
X	230	0.8	25	10.9	131	1.1	41	31.3	17	13.0	21	0.8	168	4.7
XI	310	1.1	40	12.9	129	1.1	31	24.0	6	4.4	46	1.8	133	3.8
XII	223	0.8	30	10.3	168	1.4	38	22.6	36	21.4	11	0.4	38	1.1
XIII	256	0.8	35	13.5	138	1.1	39	28.3	10	7.2	23	0.9	20	0.6
XIV	740	2.5	57	7.7	512	4.2	128	25.0	110	21.5	434	17.3	11	0.3
XV	256	0.9	29	11.3	106	0.9	28	26.4	6	5.7	64	2.6	62	1.8
XVI	233	0.8	31	13.3	91	0.8	16	17.6	5	5.5	36	1.4	5	0.1
XVII	282	1.0	29	10.3	147	1.2	47	32.0	7	4.8	33	1.3	54	1.5
XVIII	415	1.5	45	10.8	317	2.6	70	22.1	46	14.5	70	2.8	280	7.9
XIX	720	2.5	76	10.6	298	2.5	70	23.5	41	13.8	187	7.5	99	2.8
XX	366	1.3	41	11.2	192	1.6	56	29.2	24	12.5	33	1.3	64	1.8
XXI	154	0.5	11	7.3	72	0.6	12	16.7	4	5.6	42	1.7	66	1.9
XXII	235	0.8	21	8.9	105	0.9	23	21.9	9	8.6	38	1.5	144	4.1
XXIII	271	0.9	28	10.3	90	0.7	24	26.7	12	13.3	66	2.6	46	1.3
XXIV	185	0.6	19	10.3	62	0.5	12	19.4	6	9.7	18	0.7	18	0.5
XXV	116	0.4	12	10.3	114	0.9	21	18.3	26	22.8	8	0.3	25	0.7
XXVII	108	0.4	3	2.8	26	0.2	3	11.5	2	7.7	1	0.1	17	0.5
XXVIII	156	0.5	15	9.6	46	0.4	14	30.4	2	4.3	18	0.7	60	1.7
XXIX	199	0.7	19	9.5	107	0.9	25	23.4	6	5.6	31	1.2	105	2.9
XXXI	129	0.4	16	12.6	32	0.3	9	28.1	2	6.3	17	0.7	22	0.6
XXXII	58	0.2	6	10.3	22	0.2	0	....	1	4.5	4	0.2	8	0.2
XXXIII	156	0.5	11	7.1	49	0.4	11	22.4	3	6.1	12	0.5	593*	16.7*
"Accepted" types	22,895	78.5	2,697	11.8	9,011	74.8	2,028	22.3	2,185	24.2	1,375	54.9	1,068	30.1
"Higher" types	6,277	21.5	658	10.5	3,038	25.2	734	24.2	331	10.9	1,131	45.1	1,882	53.2
Total	29,172	100.0	3,355	11.5	12,049	100.0	2,762	22.9	2,516	20.9	2,506	100.0	3,543	100.0

* Not I-XXXII (not included in "higher" types) represent 16.7 per cent of the total number of carriers.
Unclassified organisms are not listed in the other columns.
"Accepted" types include I, II, III, IV, V, VII, VIII and XIV. All others are included as "higher" types.
Type XXVI is included with type VI, and type XXX is included with type XV.

38. Straker, E.; Hill, A. B., and Lovell, R.: A Study of the Nasopharyngeal Bacterial Flora of Different Groups of Persons Observed in London and Southeast England During the Years 1930-1937, Rep. Pub. Health & M. Subj. No. 90, Ministry of Health, London, His Majesty's Stationery Office, 1939.

39. Gundel, M., and Seitz, L.: Die Pneumokokkentypen in der gesunder Bevölkerung, Klin. Wchnschr. **12**: 929-932 (June 17) 1933. Gundel, M.: Bakteriologische und epidemiologische Untersuchungen über die Besiedlung der oberen Atmungswege Gesunder mit Pneumokokken, Ztschr. f. Hyg. u. Infektionskr. **114**: 659-677, 1933.

40. Footnotes 38 and 39.

41. Footnotes 29, 30 and 31.

42. Footnotes 32, 33 and 34.

Data concerning the immune response of patients with pneumonia of the "higher" types are very scant. Two series of cases in which specific antiserums were not used[43] were studied at the Boston City Hospital. Homologous type specific antibodies for "higher" types were demonstrated by the agglutination test in 17 of 51 patients tested (33 per cent). By contrast, about three fourths of all pneumonias with the "accepted" types developed agglutinins.[44] Positive tests were obtained in patients with eleven of the sixteen "higher" types represented among these 51 patients; tests were done on only 6 patients of the five types (X, XIII, XV, XXI and XXII) in which totally negative results were obtained. In six other Cooper types (XXIII, XXIX, XXV, XXVII, XXVIII and XXXII) no cases were studied.[44a] These findings may be interpreted as indicating that either (1) a large percentage of the cases of higher types are not etiologically related to the pneumonias in which they are found or (2) the "higher" types are less antigenic in addition to being less invasive, even when they are the cause of pneumonia or (3) the test used for demonstrating the antibody of these types is inadequate. Probably each of these factors is important and may be responsible, in different degrees, for the results in the various "higher" types.

Acquaintance with the relative frequency with which the various types occur in an etiologic relationship to pneumonia can serve as a diagnostic aid when one is confronted with a given case in which a pneumococcus of a given type is found only in a sputum or throat culture. Such information, however, should be used only in about the same manner as the knowledge of the relative frequency with which any given symptom, sign or laboratory finding is used in the differential diagnosis of various diseases. In the same manner it is also useful in multiple infections, either with more than one type of pneumococcus or with pneumococci and other respiratory pathogens.

In any given case of pneumonia the finding of some type of pneumococcus in cultures of the blood, lung or pleural fluid, or in cultures from some other purulent focus, may be considered as establishing the etiologic relation of that type to the pneumonia. The direct typing of sputum by the Neufeld method also permits of a relatively certain etiologic diagnosis from this source, provided (1) the sputum is obtained during the period of active infection, (2) one is reasonably certain that it was raised from the lower respiratory tract and did not come from the nasopharynx and (3) the pneumococcus of the type in question is seen either (*a*) as the only or predominant organism in characteristic "rusty" sputum or (*b*) in large numbers and as the predominant organism in purulent sputum.

43. Winkler, A. W., and Finland, Maxwell: Antibody Response to Infections with the Newly Classified Types of Pneumococci (Cooper), J. Clin. Investigation **13**: 109-120 (Jan.) 1934. Finland, Maxwell; Spring, W. C., Jr., and Lowell, F. C.: Immunological Studies on Patients with Pneumococcic Pneumonia Treated with Sulfapyridine, ibid. **19**: 179-199 (Jan.) 1940.

44. Finland, Maxwell, and Sutliff, W. D.: Specific Cutaneous Reactions and Circulating Antibodies in the Course of Lobar Pneumonia, J. Exper. Med. **54**: 637-652 (Nov.) 1931. Finland, Maxwell; Strauss, Elias, and Peterson, O. L.: Antibody Response of Patients with Pneumococcic Pneumonia Treated with Sulfadiazine and Sulfathiazole, Ann. Int. Med. **16**: 1-16 (Jan.) 1942. Winkler and Finland.[43] Finland, Spring and Lowell.[43]

44a. In infants and children also homologous, type specific antibodies can be demonstrated with greater regularity in pneumonias of the "accepted" types than in those associated with "higher" types of pneumococci. (Finland, Maxwell; Shuman, H. I., and Barnes, M. W.: The Type Specific Agglutinin Response of Infants and Children with Pneumococcus Pneumonias, J. Immunol., to be published.)

THE USE OF THERAPEUTIC ANTISERUMS IN PNEUMOCOCCIC PNEUMONIAS OF THE "HIGHER" TYPES

The early attempts to prepare therapeutic antiserums against pneumococci of the new Cooper types met with variable success.[14] There were wide variations in antibody titer, as measured by the agglutination and the mouse protection tests, both among the various types and among different horses immunized with the same type. Furthermore, the great differences in virulence of the new types of pneumococci introduced additional problems in standardization of potency. There were many other technical difficulties and costly procedures involved in the preparation of these serums which need not be detailed here. Eventually it became possible for certain laboratories to produce horse serums of reasonably uniform and high potency against a few of these types. Therapeutic trials with horse antiserums for types V and VII and then for types IV and VIII, though comparatively limited, yielded results which were sufficiently encouraging to warrant acceptance by the Council. Antipneumococcus horse serums for some of the other types were probably of equal value, but they had not been developed to the point of acceptance by the Council at the time when the use of rabbit serum was proved feasible.

In rabbits it was found possible to produce antiserums against all the specific types of pneumococci. These rabbit serums proved to be more specific and they were more uniformly of higher potency than those produced in horses and were therefore more suitable than the latter for the less frequent and so-called higher types. In early therapeutic trials, severe untoward reactions were encountered which eventually became less frequent as experience was gained in processing these rabbit serums. Those now available give rise to untoward reactions of the nonspecific varieties[45] with no greater frequency and probably much less often than the antipneumococcus horse serums produced by the same manufacturers.[46] True allergic or anaphylactic reactions are distinctly less frequent with the rabbit serums.[46] Clinical trials soon indicated that, at least for the common types for which horse serums had been accepted, namely types IV, V, VII and VIII, the serums prepared in rabbits merited acceptance by the Council. In addition, data were soon submitted which led the Council to accept antipneumococcus serums for types III and XIV.[1]

There are a number of reasons why the establishment of the true therapeutic efficacy and usefulness of antipneumococcus serums for the "higher" types is more difficult than with the types just mentioned: 1. The multiplicity of the types, the relative infrequency with which each of them is encountered and the great expense involved in making the serums has made it difficult to keep adequate stocks of serum for all types readily available in all places where they might be immediately accessible. 2. Because the higher types are so frequently associated with atypical pneumonias and with other serious diseases and conditions ("secondary" pneumonias), they are less likely to be considered for treatment early in the course of the infection, when they might be expected to exert their maximum beneficial effects. 3. The difficulties in establishing the etiologic relation-

45. Rutstein, D. D.; Reed, E. A.; Langmuir, A. D., and Rogers, E. S.: Immediate Serum Reactions in Man: Classification and Analysis of Reactions to Intravenous Administration of Antipneumococcus Horse Serum in Cases of Pneumonia, Arch. Int. Med. **68**: 25-56 (July) 1941.

46. Personal communications to the author from Dr. D. D. Rutstein and Dr. W. D. Sutliff.

ship of these types to the pneumonia are greater than with the "accepted" types. Because of their lower virulence and invasiveness, positive results of blood cultures or of cultures from lung or pleural fluids are less frequent, and fewer organisms are usually found in the sputum. Furthermore, the "higher" types occur more often as multiple infections in cases of pneumonia and are also more frequent among the organisms which constitute the common flora of the upper respiratory tract. 4. Even more important than any of the foregoing is the fact that chemotherapeutic agents in the form of sulfonamide compounds which are highly effective in pneumococcic pneumonias of all types became available at about the same time as the therapeutic rabbit serums for the higher types.

The use of sulfapyridine and, more recently, of sulfathiazole and sulfadiazine has spread rapidly and has essentially replaced the use of specific serums in all but a small percentage of the cases of pneumococcic pneumonia. It was natural, in view of the greater difficulties involved in the use of serums for the higher types, that proportionally even fewer of these cases would be treated with serums as compared with those of the more common of the Cooper types. By its very nature, the present chemotherapy is much less expensive than antiserums and, as experience with it has increased, its control has required much less effort on the part of the physician and probably involved less risk to the patient. The toxic reactions, which were quite significant with the use of sulfapyridine, have become less frequent and less severe with the advent of the successive compounds sulfathiazole and sulfadiazine, while the recognition and management of those reactions which occur has become a less serious problem. The wide range of effectiveness of these drugs had made possible the early initiation of treatment—a highly important factor in the success of any specific measure in pneumonia. This, in turn, has made early and rapid etiologic diagnosis less important and, for practical purposes, it has gradually been dispensed with by a large majority of physicians. Except where special interests in the problem required a continuation of the diagnostic efforts, typing has been reserved in large part for those cases in which chemotherapy is not entirely successful or for certain selected cases, usually the severest ones. This is unfortunate, since it is in just such cases that early etiologic diagnosis is most desirable.

These facts could not easily be ignored by any physician who attempted to conduct therapeutic trials with specific serums. It would, of course, be highly desirable to have a number of large and carefully controlled series of cases in which specific serum, chemotherapy and the combination of the two were applied to patients in strict rotation. The nature of these forms of treatment, however, and the numerous difficulties involved in conducting such clinical experiments have been sufficient to discourage most workers. Some early attempts to conduct such trials on a limited scale by alternating cases between serum therapy and chemotherapy indicated that specific serums in selected cases of lobar pneumonia yielded therapeutic results which, in most respects, were comparable to those obtained in corresponding cases treated with sulfapyridine.[47] Subsequent studies of this sort were aimed at comparing the value of chemotherapy when used alone and in combination with specific serums.[48] Attempts at strict alternation of cases on such a basis when it also permits of the immediate use of drug alone, although it may at first glance appear to be the preferable method, raises a number of problems which render the results open to considerable criticism. These problems are discussed elsewhere, together with a critical review of the results of therapeutic experiments with specific serums in general and with antipneumococcus serums in particular.[49]

From a practical point of view it seems quite futile to discuss the relative merits of serum and sulfonamide compounds when used separately or in combination. There is no longer any question of adopting any one of these methods of treatment as a routine to the exclusion of the other methods, unless it be the use of chemotherapy alone. The latter is, and probably will continue to be, the treatment of first choice in all except a relatively small percentage of cases. Obviously the expense, time, effort and risks of serum therapy would then be undertaken only for possible added benefits or to avoid greater risks that might be involved in chemotherapy. The essential problems, therefore, are to determine (1) under what conditions specific serums add materially to the chances of recovery or significantly reduce the period of acute illness and (2) whether there are any conditions in which serum might advantageously be used instead of a sulfonamide compound. Answers to these problems are difficult to obtain and, in my opinion, they lie in a thorough study of a large number of consecutive individual patients[50] and will necessarily vary according to the personal experience of the investigator.

MORTALITY RATES AND THEIR INTERPRETATION

With all the foregoing factors in mind, an attempt was made to collect from various accessible sources those groups of cases in which (1) typing was carried out for all the Cooper types, (2) reasonably large numbers of cases were available and (3) the various forms of treatment under discussion were used. Since the immediate problem was the determination of the usefulness of the "higher" types of rabbit antipneumococcus serums, the data in the various therapeutic groups were essentially limited to cases treated since the summer of 1938. Contemporaneous cases treated without serums or sulfonamide compounds were available from some of the same sources, but a number of earlier cases in this category were also included in order to obtain a better approximation to the basic mortality in the pneumonias of the various types uninfluenced by either serum or chemotherapy. The cases in the various therapeutic groups are obviously not comparable. They are merely useful in determining, as nearly as possible, the mortality rates in each group under the conditions in which the therapy was employed.

The mortality rates in the collected series of cases receiving each form of treatment are shown for the

47. (a) Dowling, H. F., and Abernethy, T. J.: The Treatment of Pneumococcus Pneumonia: A Comparison of the Results Obtained with Specific Serum and with Sulfapyridine, Am. J. M. Sc. **199:** 55-62 (Jan.) 1940. (b) Ruegsegger, J. M.; Hamburger, Morton, and Cockrell, Sarah L.: The Comparative Use of Sulfapyridine and Specific Serum in Pneumococcal Pneumonia, Ohio State M. J. **36:** 257-261 (March) 1940.

48. Dowling, H. F.; Abernethy, T. J., and Hartman, C. R.: Should Serum Be Used in Addition to Sulfapyridine in the Treatment of Pneumococcic Pneumonia? J. A. M. A. **115:** 2125-2128 (Dec. 21) 1940. Carey, B. W.: The Treatment of Pneumonia in Infants and Children, J. Pediat. **18:** 153-161 (Feb.) 1941. Plummer and others.[50]

49. Finland, Maxwell: Controlling Clinical Therapeutic Experiments with Specific Serums with Particular Reference to Antipneumococcus Serums, New England J. Med. **225:** 495-506 (Sept. 5) 1941.

50. Finland, Peterson and Strauss.[64] Finland.[49]

individual types in table 3.[51] Unfortunately, it is not possible to obtain adequate information concerning the reasons for the choice of therapy in most instances, since this factor alone may have greatly influenced the mortality rates. It is interesting to note, however, the relative proportion of cases in each therapeutic group which are of the "higher" types. Of the 9,053 cases treated with serum alone 688, or 7.6 per cent, were of the higher types; of the 12,167 cases treated with both serum and sulfonamide compounds 2,248, or 18.6 per cent, were of the higher types; among the 12,547 cases treated with chemotherapy alone 4,337, or 34.6 per cent, were of the higher types; and among the 8,101 cases in which neither serum nor drug was administered 2,812, or 28.8 per cent, were of the higher types. At least one reason for the small proportion of "higher" type cases among those treated with serum is the fact that serums for these types were less readily available than those for the "accepted" types. A few relevant points concerning each of the therapeutic groups may be noted.

Cases Treated with Serum Alone.—In this group the mortality in the cases of the "Council accepted" types probably corresponds to the average of the results reported prior to the advent of effective sulfonamide compounds. In a large proportion of these cases horse serums were administered; this was particularly true of the cases of types I, V and VII and somewhat less so of types II, IV and VIII. In almost all of the type III and type XIV cases, however, rabbit serums were administered. Individual reports of appreciable numbers of cases in which rabbit serums were used exclusively have shown much lower mortality figures, although the cases were of average or greater than average severity.[52] For example, Loughlin, Bennett and Spitz[53] had only 3 deaths among 125 patients (2.3 per cent) with types V, VII and VIII pneumococcus pneumonia, of which 30 per cent gave positive blood cultures. Crisis occurred within a few hours in 82 per cent of these patients after a single dose of serum was administered. MacLeod[54] reported 4 deaths among 74 cases (5.4 per cent) other than those of type III. These results are comparable with the best results from chemotherapy in similar cases. Furthermore, these two reports include cases collected before chemotherapy was used. For the majority of the cases listed in the table, however, it must be borne in mind that, since effective chemotherapy was available, probably drugs in addition were employed in some of the severer cases and these are therefore taken out of this group.

The serum treated cases of the higher types fall into four groups. The first includes cases of types XII, XX, XXV and XXVII in which the mortality was lower than in the corresponding cases in the other therapeutic groups. The second group includes cases of types IX, X, XVII, XVIII, XXIV and XXXIII. In each of these types the mortality was less than 15 per cent and was comparable, in general, with the results in serum treated cases of the "accepted" types. The relative mortalities in this group, when compared with the corresponding mortality rates in the other therapeutic groups, were also similar to those of the "accepted" types. In these two groups of types it is fair to assume that serum exerted a definite beneficial effect on the mortality rates. In some of these types, and in others of the serum treated cases, the numbers of cases are small and the significance of the fatality rates may therefore be open to question.

The third group includes types VI, XIX, XXII, XXIII, XXIX and XXXII, in which the mortality was higher in the serum treated cases than in the other two therapeutic groups but was lower than in the cases of the corresponding types in which neither serum nor sulfonamide derivatives were used. In this group possibly some benefit resulted from the serum treatment, although this cannot be determined without further data bearing on the choice of cases. In the last group, which includes types XI, XIII, XV, XVI, XXI, XXVIII and XXXI, no possible benefit could be ascribed to the serum, at least on the basis of the mortality rates. The latter were higher than in the cases of the corresponding types treated with sulfonamide compounds alone or with serum, or in those in which neither therapy was used. The number of cases of some of these types, however, was quite small.

The mortality in the whole number of cases of the higher types that were treated with serum alone was greater than that of the "accepted" types. The mortality in the former was about two thirds, and in the latter less than one half of that of the corresponding types among the cases in which neither serum nor sulfonamide compounds were employed.

Among all the serum treated cases one must reckon with the possibility that many of them were included for this treatment alone because of complications which precluded the use of sulfonamide compounds. The prognosis for recovery from pneumonia in some cases of this sort is very poor, as, for example, in those with severe renal or hepatic disease or after extensive abdominal operations.

An appreciable number of the earlier cases included among those in which serum alone was used were treated before the advent of sulfapyridine or they were collected in the course of studies which precluded the use of drugs. Furthermore, a number of these cases were treated during the developmental stage of rabbit serum therapy and lots of serum for clinical trial were employed before they were released for general use. Some of these lots were of relatively low potency and gave severe untoward reactions.

The problem of subtypes that has been discussed must be considered especially in relation to the results

51. The data in this table were derived from the following sources: Boston City Hospital (Finland, Spring and Lowell[34] and Finland, Lowell and Strauss[34]), Harlem Hospital (data furnished by Dr. Bullowa) and the health departments of New York State,[20] Illinois[20] and Pennsylvania.[21] Additional cases treated with serum alone are from the Rockefeller[54] and Cook County (Volini, I. F., and Levitt, R. O.: The Treatment of Pneumococcic Pneumonia with Concentrated Rabbit Serum, J. A. M. A. **113**: 1314-1316 [Sept. 30] 1939) hospitals and from the Danish Serum Institute (Nissen, N. I.: Serum Treatment of Pneumonia in Denmark, Acta med. Scandinav. Supp. **123**: 16-35, 1941), and a number supplied in personal communications from Drs. Harry F. Dowling, Washington, D. C.; John W. Brown, San Francisco, and Roscoe L. Mitchell of the Bureau of Health of the State of Maine. Additional cases treated with serum and sulfonamide compounds are from St. Louis (Sigoloff, Emanuel: The St. Louis Pneumonia Control Program: A Statistical Evaluation of Various Forms of Therapy, J. Missouri M. A. **37**: 431-435 [Oct.] 1940), New York City (personal communications from Dr. W. D. Sutliff) and Bellevue Hospital.[23] Additional cases treated with sulfonamide compounds alone are from Bellevue Hospital,[23] Philadelphia (Pepper, D. S.; Flippin, H. F.; Schwartz, Leon, and Lockwood, J. S.: The Results of Sulfapyridine Therapy in Four Hundred Cases of Typed Pneumococcic Pneumonia, Am. J. M. Sc. **198**: 22-35 (July) 1939. Flippin, H. F.; Rheinhold, J. G., and Schwartz, Leon: Sulfapyridine and Sulfathiazole Therapy in Pneumococcic Pneumonia, J. A. M. A. **116**: 683-689 [Feb. 22] 1941), Washington, D. C.,[47a] and Cincinnati, Ohio.[47b] All these cases are contemporaneous and occurred from 1938 to 1941. Earlier cases in adults not treated with serum or sulfonamide compounds were obtained from the Boston City[20] and Harlem hospitals (Bullowa: The Management of the Pneumonias[27] and personal communication to the author).

52. MacLeod,[54] Loughlin, Bennett and Spitz.[53]

53. Loughlin, E. H.; Bennett, R. H., and Spitz, S. H.: The Treatment of Types V, VII and VIII Pneumococcus Pneumonia with Rabbit Antipneumococcus Serum, New York State J. Med. **39**: 1713-1721 (Sept. 15) 1939.

54. MacLeod, C. M.: Treatment of Pneumonia with Antipneumococcal Rabbit Serum, Bull. New York Acad. Med. **15**: 116-124 (Feb.) 1939.

obtained in types IX, X, XI, XV, XVI and XVIII. Some, at least, of the poor results obtained in cases of these types were very probably attributable to this cause.[55] In the preparation of most of the recent lots of serums, cognizance is taken of the subtypes, and antibodies for some of them are included in the therapeutic serums.

In the evaluation of specific curative agents in the treatment of pneumococcic pneumonias, the effect on the clinical course may be considered of almost equal importance with the reduction in the mortality rates. This is particularly true when only small numbers of cases are available. Almost every one of the writers who has reported on the serum treatment of any appreciable number of cases has emphasized the fact that recovery by crisis following homologous type specific serum treatment of the higher type cases is usually as rapid and as dramatic as in the cases of the more common or "accepted" types.

Cases Treated with Serum and Sulfonamide Compounds.—In evaluating the mortality in these cases it is important to bear in mind that only a small proportion of them received the combined treatment from the start. Furthermore, most of those in whom the two kinds of treatment were begun at the same time or within a short time of each other probably represent the poorest risks. For the most part, this group includes patients to whom chemotherapy was given first and then serum was used after a varying interval because either (1) the response to the drug did not seem adequate, (2) the drug produced toxic effects which interfered with the continuation of adequate treatment or (3) new data indicating a poor prognosis (positive blood culture, evidence of a spreading pneumonic lesion and so on) became available before adequate improvement had taken place from the drug. A small number of these patients received serum first and then were given chemotherapy because of an inadequate response to the serum or because of the finding of a mixed infection or of some other complication. It is to be expected, therefore, that these cases should include the highest percentage of cases of the worst prognostic groups, namely those in the oldest age groups, those with positive blood cultures or multiple lobe involvement[56] and also many "secondary" and atypical pneumonias.[57]

For the most part, the mortality for each type in the cases treated with serum and sulfonamide compounds is quite comparable to that found in the corresponding cases treated with serum alone, considering the small numbers of cases among the latter. Here also the mortality was greater in cases of the "higher" types than in those of the "Council accepted" types. The gross mortality in each of these two groups was slightly lower than in the corresponding cases treated

TABLE 3.—*Mortality in a Collected Series of Adult Cases of "Typed" Pneumococcic Pneumonia According to the Type of Pneumococcus and the Kind of Specific Treatment Used*

	Serum Alone			Serum and Sulfonamide Compound			Sulfonamide Compound Alone			No Serum and No Sulfonamide Compound		
Pneumococcus Type	Number of Cases	Died	Per Cent Died	Number of Cases	Died	Per Cent Died	Number of Cases	Died	Per Cent Died	Number of Cases	Died	Per Cent Died
I	4,512	596	13.2	3,456	315	9.1	2,012	100	5.0	1,084	334	30.8
II	992	223	22.5	1,466	177	12.1	1,095	69	6.3	513	208	40.5
III	317	90	28.4	1,687	343	20.3	1,681	219	13.0	1,290	544	42.2
IV	237	34	14.3	512	86	16.6	605	34	5.6	403	104	25.8
V	631	77	12.2	468	52	11.1	572	29	5.1	517	162	31.3
VII	863	98	11.3	1,082	110	10.2	959	49	5.1	577	138	23.9
VIII	635	89	14.2	941	126	13.4	790	45	5.7	723	158	21.9
XIV	118	13	11.0	307	39	12.7	496	39	7.7	282	93	33.0
"Council accepted" types	8,305	1,220	14.7	9,919	1,248	12.6	8,210	583	7.1	5,389	1,741	32.3
VI	121	25	20.7	302	55	18.2	598	33	5.5	298	72	24.2
IX	41	6	14.6	144	19	13.2	195	16	8.2	229	62	27.1
X	17	2	11.8	86	13	15.1	152	14	9.2	161	50	31.1
XI	36	12	33.3	120	16	13.3	177	21	11.9	146	36	24.7
XII	40	1	2.5	82	13	15.9	173	22	12.7	173	48	27.7
XIII	17	7	41.2	80	17	21.3	194	20	10.3	137	37	28.0
XV	23	7	30.4	69	8	11.6	208	21	10.1	85	25	29.4
XVI	25	6	24.0	77	15	19.5	152	18	11.8	89	19	21.3
XVII	25	3	12.0	106	14	13.2	267	22	10.6	144	54	37.5
XVIII	62	8	12.9	169	32	19.0	298	32	10.7	251	68	27.1
XIX	92	19	20.7	278	47	16.9	466	34	7.3	253	63	24.9
XX	23	1	4.3	127	25	19.7	253	21	8.3	207	65	31.4
XXI	8	2	25.0	45	7	15.6	120	6	5.0	69	10	14.7
XXII	19	3	15.8	83	16	19.3	161	13	8.1	98	21	21.4
XXIII	18	3	16.7	95	20	21.1	181	13	7.2	98	23	23.5
XXIV	17	2	11.8	59	12	20.3	129	7	5.4	48	11	22.9
XXV	23	2	8.7	58	14	24.1	123	14	11.4	63	11	17.5
XXVII	9	0	0.0	35	3	8.6	79	2	2.5	37	4	10.8
XXVIII	8	3	37.5	53	11	20.8	104	9	8.7	49	11	22.4
XXIX	25	5	20.0	64	9	14.1	143	16	11.2	96	23	24.0
XXXI	18	5	27.8	46	5	10.9	70	7	10.0	39	10	25.6
XXXII	6	1	16.7	21	2	9.5	34	3	8.8	26	3	11.5
XXXIII	15	2	13.3	49	9	18.4	120	8	6.7	21	5	23.8
"Higher" types	688	125	18.2	2,248	382	17.0	4,337	372	8.6	2,812	731	26.0
Total	9,053	1,345	14.9	12,167	1,630	13.4	12,547	955	7.6	8,101	2,473	30.5

Type XXVI is included with type VI, and type XXX is included with type XV.
Type XXXIII is listed because therapeutic serum was available for most of the period covered.
The large majority of patients were adults. The "state" cases include infants and children. The latter are estimated to constitute less than 5 per cent of the patients treated with serum, either alone or with chemotherapy, about 15 per cent of those treated with sulfonamide compounds alone and about 10 per cent of those receiving no specific treatment.
Horse serums were used in a considerable proportion of the patients with types I, II, V and VII and in a small number of those with IV and VIII. Rabbit serums were used in almost all the remaining cases.
The sulfonamide compounds used include chiefly sulfapyridine, sulfathiazole and sulfadiazine or their sodium salts.

55. Davidson and Bullowa.[7] Carey.[48]

56. Rosi, Sagen and Prange.[50] Finland, Spring and Lowell.[54] Finland, Lowell and Strauss.[54]

57. Finland, Spring and Lowell.[54] Finland, Lowell and Strauss.[54]

with serum alone. This differs from some of the results previously reported from large hospitals, in which the mortality was appreciably higher in the cases in which combined therapy was given. Much of the difference, as will appear later, is due to the inclusion of cases treated in statewide programs in which the greater use of serums was facilitated and probably encouraged.

An evaluation of the relative effect of the combined treatment as compared with chemotherapy alone is obviously not possible from these data. Much depends on the relative numbers of cases in each of the prognostic groups.[58]

In the cases in which combined therapy was used, as in those in which serum alone was employed, the mortality rates in the cases of the various higher types were, generally speaking, similar to those obtained in the cases of the "Council accepted" types. This is of particular significance since it must be assumed, in view of what has already been said about the use of higher type serums, that more stringent indications were probably required by most physicians before undertaking to use them.

From the point of view of the clinical response, the experiences at the Boston City Hospital and those of many other observers have indicated that an appreciable proportion of the cases showed a direct response by crisis following serum, even after they had failed to improve under chemotherapy.[58] Many of the cases, however, show only moderate additional improvement immediately, and this is particularly true in the cases in which purulent complications, mixed infections or extensive pulmonary lesions were present.

TABLE 4.—*Outcome of Cases of Pneumococcic Pneumonia Treated with Antipneumococcus Serum and Sulfonamide Compounds*

(Reported to the New York City Department of Health from Oct. 1, 1940 to Sept. 30, 1941)*

Evaluation of Result	Cases of "Accepted" Types	Cases of "Higher" Types
Recovered cases (total)	510	114
1. Temperature normal 48 hours after therapy and thereafter	80	13
2. Striking effect on temperature in 48 hours, but specified incomplete; or time or completeness not specified	90	26
3. Striking effect after serum; not after chemotherapy	32	11
4. Striking effect after chemotherapy; not after serum	0	0
5. Lack of effect demonstrated (adequate treatment for 3 days)	10	2
6. Recovery; not 1, 2, 3, 4, or 5 or not described	298	62
Deaths (total)	126	56
1. Less than 24 hours after therapy	15	7
2. More than 24 hours after therapy	111	49
Grand totals	636	170

* Data supplied by Dr. W. D. Sutliff, assistant director (pneumonia), Bureau of Laboratories.

Thus, it is seen in table 4 that, in most of the cases treated in New York City with both serum and drugs and in which data are available, specific serums probably contributed to the recovery. The proportion of cases of the "higher" types that probably benefited from serum was essentially the same as in those of the "accepted" types. An evaluation of the effect of serum in the "higher" type cases treated at the Boston City Hospital is shown in table 5. In the recovered cases, serum was considered to have a definite beneficial effect in most instances.

Cases Treated with Sulfonamide Compounds but Without Serum.—The mortality in these cases was lower than for each of the other therapeutic groups

TABLE 5.—*Evaluation of the Clinical Effect of Specific Antiserum in Patients with "Higher" Type Pneumococcic Pneumonia or Meningitis*

Boston City Hospital, 1938-1941

Evaluation of Result	Pneumonias: Serum Alone	Pneumonias: Serum and Sulfonamide Compound	Meningitis,* Serum and Drug
Recovered cases, total	28	20	20
1. Severe cases, excellent or good response attributable to serum	17	11	19
2. Good or fair response, role of serum indeterminate	9	9	1
3. No obvious effect from serum	2	0	0
Fatal cases, total	6	12	42
1. Treatment with serum begun while patient was moribund	2	5	22
2. Adequate trial but no apparent benefit from serum	0	2	3
3. Temporary improvement attributable to serum (including cases with endocarditis or death due to other causes)	4	5	17
Grand total	34	32	62

* A few of these cases were obtained from reports made to the Antitoxin and Vaccine Laboratory of the Massachusetts Department of Health and were furnished by Dr. Geoffrey Edsall, acting director.

and this was true for almost all types. Most of these cases are from sources where serums were also used to a greater or lesser extent. It must be assumed, therefore, that the lower mortality is attributable, at least in part, to the use of serum in some of the severe cases. This inevitably excludes an appreciable proportion of cases from the "drug alone" group and includes them under the combined therapy. As a result the case fatality rates in the latter are increased, and those in the former are decreased proportionally.

It is of interest that the mortality in the various higher types was, for the most part, appreciably higher than in the "accepted" types. The mortality in all the latter cases, after excluding those of type III, was 5.6 per cent. A lower mortality was noted in only 4 of the higher types (VI, XXI, XXIV and XXVII). From what has been said previously, this is probably the result of the inclusion of a greater proportion of atypical and "secondary" pneumonias among the cases of the higher types that were treated only with drugs.

Cases in Which No Serum and No Sulfonamide Compounds Were Administered.—Over two thirds of all these cases occurred before rabbit serums or effective sulfonamide compounds became available. The mortality rates, at least in the cases of the higher types, therefore represent a fair approximation of the basic mortality in cases of these types uninfluenced by serums or chemotherapy. The mortality rates in the higher types in this group were generally lower than in "Council accepted" types.

THE CHOICE OF CASES FOR THE VARIOUS FORMS OF THERAPY AND ITS EFFECT ON MORTALITY

It is obvious from what has been said that the proportions of cases of the various prognostic groups that are chosen for each kind of therapy will, in a large measure, determine the case fatality rate in all the

58. Finland, Spring and Lowell.[34] Finland, Lowell and Strauss.[34] Finland, Peterson and Strauss.[64]

cases in which that kind of therapy is employed. This does not take into account the reasons for choosing some particular therapy in the individual cases, and these may be of similar importance. When multiple therapy is used, the estimation of the various prognostic factors alone, for instance, by "adjusted fatality rates," [30] though indicating the greater severity of the cases chosen, does not fully reflect the additional value of the second therapy used.[59] In the cases from Illinois [30] it was shown that the cases in which combined therapy was used included a larger proportion of those in the worst prognostic groups. This was also true at the Boston City Hospital [57] and probably wherever the combined treatment has been used. In table 6 are shown the case fatality rates from various kinds of treatment in the cases from Illinois and from two large hospitals. The latter were chosen because they represent cases that were studied in a more uniform manner and also because the results of blood cultures were available in almost all of the cases. The effect of this factor alone on the choice of therapy and on the resulting fatality rates can thus be estimated. Cases of the "higher" and of the "accepted" types are also compared.

The outstanding differences in the choice of cases in these two series is the higher proportion of cases from Illinois in which the combined treatment was used and the higher proportion of hospital cases in which neither serum nor sulfonamide derivatives were used. Serum alone was also used in an appreciably higher proportion of the hospital cases. The more frequent selection of cases for combined treatment in the Illinois series probably explains, in part at least, the lower mortality in this group of cases as compared with the cases in which serum alone was used, whereas in the hospital group the more rigid selection of cases for combined treatment resulted in a relatively higher fatality rate with this therapy.

In both series, relatively more cases of the "accepted" types than of the higher types were treated with serum, either alone or with drugs. The reverse was true for the cases treated with drug alone, as might be expected. This form of treatment was used in a greater proportion of the higher type cases. The fatality rates in all the cases of the higher types were slightly higher than those of the accepted types in the corresponding therapeutic groups of both series, except for the group with no serum or drug in the Illinois series.

TABLE 6.—*Mortality and Distribution of Cases of "Accepted" and of "Higher" Types of Pneumococcic Pneumonia According to the Kind of Treatment Used in Two Selected Series*

		Boston City Hospital 1938-1940 and Harlem Hospital 1938-1941								Illinois 1938-1941			
						Per Cent with Positive Blood Cultures	Cases with Positive Blood Cultures						
Pneumococcus Types	Specific Therapy	Number of Cases	Per Cent of Cases	Died	Per Cent Died		No. of Cases	Per Cent of Cases	Died	Per Cent Died	No. of Cases	Per Cent of Cases	Died	Per Cent Died
"Council accepted" types	Serum	535	19.9	63	11.8	21.0	117	21.4	42	35.9	848	9.8	102	12.0
	Serum and sulfonamide compounds	610	22.7	97	15.9	32.1	193	35.2	69	35.8	4,814	55.3	490	10.2
	Sulfonamide compounds	1,118	41.6	144	12.9	17.9	200	36.5	64	32.0	2,708	31.8	132	4.8
	No serum, no sulfonamide compounds	425	15.8	113	26.6	8.9	38	6.9	36	94.7	271	3.1	59	21.8
	Total	2,688	100.0	417	15.5	20.4	548	100.0	211	38.5	8,701	100.0	783	9.0
"Higher" types	Serum	118	9.3	16	13.6	10.2	12	13.6	2	16.7	172	4.1	41	23.8
	Serum and sulfonamide compounds	82	6.5	26	31.7	22.0	18	20.5	9	50.0	1,531	36.6	200	13.1
	Sulfonamide compounds	465	36.6	98	21.1	6.0	30	34.1	9	30.0	2,153	51.5	111	5.2
	No serum, no sulfonamide compounds	605	47.6	176	29.1	4.6	28	31.8	27	96.4	326	7.8	42	12.9
	Total	1,270	100.0	316	24.1	6.9	88	100.0	47	52.4	4,182	100.0	394	9.4
All types	Serum	653	16.5	79	12.1	19.8	129	20.3	44	34.1	1,020	7.9	143	14.0
	Serum and sulfonamide compounds	692	17.5	123	17.7	30.5	211	33.2	78	37.0	6,345	49.2	690	10.9
	Sulfonamide compounds	1,583	40.0	242	15.3	14.5	230	36.1	73	31.7	4,921	38.2	243	4.9
	No serum, no sulfonamide compounds	1,030	26.0	289	28.1	6.4	66	10.4	63	95.5	597	4.7	101	16.9
	Total	3,958	100.0	733	18.5	16.3	636	100.0	258	40.6	12,883	100.0	1,177	9.2

The term "sulfonamide compounds" here refers to sulfapyridine, sulfathiazole or sulfadiazine.

In the hospital series the high fatality rates in the cases with combined therapy are associated with a correspondingly high incidence of positive blood cultures. This was true both in the cases of the "accepted" types and in those of the higher types. The mortality in all the "treated" bacteremic cases was quite similar regardless of whether serum, drug or both were used. The apparent differences noted under the various forms of therapy in the cases of higher types may be due to the small numbers of cases involved. Among the bacteremic cases, the proportion of those chosen for combined therapy (33.2 per cent) was almost twice as great as in the entire group (17.5 per cent), and for the cases of the higher types it was three times as great (20.5 and 6.5 per cent respectively). The incidence of positive blood cultures in the treated cases was highest in those receiving combined treatment and lowest in those treated only with drugs. Bacteremia, as expected, was more frequent in the cases of "accepted" types than in those of the "higher" types.

Results in Infants and Children.—Data for evaluating the effects of specific serums in infants and children are very scant. The various "state" series include considerable numbers of cases in the lower age groups,

59. For example let us assume that the expected case fatality rate in cases of type I pneumonia in the fifth decade of life, with bacteremia and a single lobe involved, is 50 per cent. If we then begin with 100 such patients and give them all chemotherapy, it is fair to assume that the great majority of the 50 patients who would eventually have recovered without specific therapy would respond fairly promptly to chemotherapy alone. If we assume that 40 patients responded in this manner to a sulfonamide derivative, there would remain 60 possible candidates for additional serum therapy after eighteen to thirty-six hours. If 50 of these 60 patients were then chosen at random and treated with serum, the highest expected death rate in the 50 cases ending up with drug alone is 20 per cent, and the lowest expected fatality rate in the 50 cases ending up with both treatments is 80 per cent and the highest possible is 100 per cent. If the actual death rate was 10 per cent in the drug alone group and 20 per cent in the combined therapy group, the maximum reduction in death rate ascribable to the drug in the former is from 20 per cent to 10 per cent and the reduction in the latter that could be ascribed to drug would be from between 80 and 100 to between 40 and 50 per cent. The additional drop to 20 per cent would then be ascribable to serum. The low fatality rate in the drug alone group, therefore, is due as much to preselection among the cases with various prognostic factors as it is to the incidence of these factors. Solely on the basis of the incidence of the prognostic factors, chemotherapy alone would here be considered to be twice as effective as the combined treatment in reducing the case fatality rate.

but those receiving serum are very few. The added difficulties of "typing," the frequency with which multiple types are encountered, the low basic mortality in children over 2 years of age and the even lower mortality rates in infants and children treated with sulfonamide compounds alone—all these factors have left but little in the way of inducements for the use of serums except in rare cases. There is therefore little information of significance concerning the use of serums of the higher types in such cases.

Carey and Cooley [60] used antipneumococcus rabbit serums in 106 cases, including those of types I, V, VII, VIII, XIV, XV, XVI, XVIII, XIX and XXIII, and found them equally effective in all these types except in 2 cases of type XVIII, which were probably subtypes or other related types. They also used sulfapyridine in 246 cases and found this drug effective in all thirty-two types. In a subsequent paper Carey [48] reported that antipneumococcus rabbit serums, combined with sulfapyridine or sulfathiazole, seem to possess a slight advantage over the use of these drugs alone. The duration of the acute disease after treatment was started was less than with chemotherapy alone, and recurrent pneumonia was not observed in the cases in which the combined treatment was used but was frequent after the drugs were used alone. In view of all the various factors involved, however, he felt that the routine administration of serum in infants and children was not practical except in the event of pneumococcic bacteremia, widespread involvement of the lungs or severe toxicity from the infection.

USE OF SERUMS IN PNEUMOCOCCIC MENINGITIS AND PERITONITIS

The use of serums in pneumococcic meningitis and peritonitis, as it concerns meningitis, has been reviewed recently and little need be said here.[61] There can be no question that almost all of the recent recoveries in this disease are ascribable directly to the use of sulfanilamide and other sulfonamide compounds, in the sense that these recoveries probably would not have occurred without the use of such drugs. In a large number of the reported cases of recovery, however, specific serum was used in addition. We are therefore confronted with the same problem as in the cases of pneumonia. In many of the cases the serum was given after an appreciable interval, during which evidence of cure with the drugs alone was not forthcoming. The finding of a similar mortality in a collected series of cases treated with drug alone and in similar cases in which serum in addition was used [37] can be interpreted only as indicating that the drugs alone are capable of bringing about recoveries, but it does not indicate the value, if any, of the serum added in those cases in which it was used. It cannot be said that the serum was of no value unless treatment with both the serum and the drug was begun together in all cases. On the other hand, it is more reasonable to suppose that the additional administration of serum helped to salvage a large proportion of the patients who were doing poorly under chemotherapy. A careful study of individual cases [62] has yielded more direct evidence of additional benefit from serum in the rapid sterilization of the cerebrospinal fluid in certain cases after chemotherapy alone had failed to bring about this result even when used intensively for a reasonable period. The high proportion of cases of pneumococcic meningitis which are of the higher types (table 1) indicates that serums for these types should find a place in the therapy of these cases.

Data on the use of serum in pneumococcic peritonitis are very scant.[63] Sulfanilamide and other sulfonamide compounds have proved effective when used alone in some of these cases, and antipneumococcus serums have been used in addition in others in which recovery occurred. The additional value of specific antiserums, while fairly well established in experimental infections in animals, is even more difficult to determine in human cases of pneumococcic peritonitis than it is in pneumonia or meningitis. The combined treatment is probably indicated, as in the latter infections, but the mortality is still high in spite of the use of both serum and drugs.

COMMENT

The two main questions that arise with respect to the antipneumococcus serums of the higher types may be stated thus: 1. Are they effective in the treatment of cases of pneumonia in which these types occur? 2. Are they useful in the treatment of pneumonia or of other pneumococcic infections now that effective sulfonamide compounds are available for the treatment of the same conditions? With respect to the second, there are really two questions involved. (*a*) Are there any conditions in which the serum might be used alone without drugs? (*b*) Are the serums of value as a supplement to the sulfonamide compounds?

The answer to the first question, as far as it concerns the great majority of the higher types, can, with reasonable assurance, be stated in the affirmative. It must, of course, be added that the effectiveness of the serums of the higher types depends on the same principles which govern the effective use of serums of the "accepted" types. They must be used in the homologous type infection and in adequate amounts. They are also most effective when given early in the course of the disease.

As far as the practical usefulness of these higher type serums is concerned, that may depend on the circumstances under which they are used. They may, of course, be of value when used alone in cases in which sulfonamide drugs cannot be tolerated. They may be resorted to in cases in which the organism is resistant to the action of these drugs or when, for this or for other reasons, there is a poor response to chemotherapy. In certain cases of great severity, as when there is bacteremia or an extending pulmonary lesion or the early development of purulent complications, these serums, when used in addition to the drug, may be of great benefit. When used in such cases, either from the start or after comparatively brief intervals of chemotherapy alone, they may play an important part in the eventual recovery or in curtailing the period of the acute illness.[64]

60. Carey, B. W., and Cooley, T. B.: Pneumonia in Infants and Children, J. Pediat. **15:** 613-620 (Nov.) 1939.

61. Dingle, J. H., and Finland, Maxwell: Diagnosis, Treatment and Prevention of Meningococcic Meningitis with a Résumé of the Practical Aspects of Treatment of Other Acute Bacterial Meningitides, War Med. **2:** 1-58 (Jan.) 1942.

62. Finland, Maxwell; Brown, J. W., and Rauh, A. E.: Treatment of Pneumococcic Meningitis: A Study of Ten Cases Treated with Sulfanilamide Alone or in Various Combinations with Specific Antipneumococcic Serum and Complement Including Six Recoveries, New England J. Med. **281:** 1033-1044 (June 23) 1938.

63. Ladd, W. E.; Botsford, T. W., and Curnen, E. C.: Primary Peritonitis in Infants and Children, J. A. M. A. **113:** 1455-1459 (Oct. 14) 1939. Sager, W. W.: Treatment of Pneumococcal Peritonitis with Sulfamido Drugs and Serum; Report of Two Cases, Med. Ann. District of Columbia **9:** 81-82 (March) 1940. Pahmer, Marcel: Pneumococcus Peritonitis in Nephrotic and Non-Nephrotic Children, J. Pediat. **17:** 90-106 (July) 1940.

64. Finland, Maxwell; Peterson, O. L., and Strauss, Elias: Some Uses and Abuses of Chemotherapy in Pneumonia, New England J. Med. **225:** 601-607 (Oct. 16) 1941.

The fact that the mortality in cases of pneumonia of the higher types is still comparatively high with the use of chemotherapy alone may be a reflection of the severity of the host factors involved in these cases. It may also be interpreted as indicating that the part played by the pneumococcic infection is not entirely overcome by the drugs alone and, at least in some of these cases, serum may have a significant part to play. The proportion of cases of the higher types in which serums may be useful is difficult to evaluate, but it is probably quite small.

These statements hold true for cases of pneumonia, in which there are often difficulties in establishing the etiologic relationship of the higher type pneumococcus to the disease. In cases of pneumococcic meningitis or peritonitis, on the other hand, the etiologic significance of the organism found is not in doubt. The proper use of specific serums in such cases may be considered of great value and should be encouraged. Since an appreciable proportion of such cases, at least those of meningitis, are caused by pneumococci of the higher types, it would seem highly desirable that potent serums for these types be available.

SUMMARY AND CONCLUSIONS

Many new types of pneumococci have been added to the original types I, II and III and the Cooper types IV to XXXII. A few of the newer types have been found to be of significance in disease, but many of these have been shown to be closely related to the previously classified types. With respect to diagnosis and treatment, however, the difficulties introduced by these types can be and, in part, have been minimized by the preparation of both diagnostic and therapeutic serums which cover the groups of related types.

All of the types I to XXXII and most of the newer ones have been found to be etiologically related to pneumonia and other infections, and they have all been found in healthy carriers who have had no known contact with such infections. The relative frequency with which each of the various types is found to be pathogenic varies considerably. The "higher" types, on the whole, have been found to be less invasive than the "Council accepted" types (I. II. III. IV, V, VII, VIII and XIV). This varies considerably for the individual higher types, however, and a few of them have proved to be as invasive as some of the Council accepted types.

The mortality in the pneumonias associated with each of the higher types does not bear any apparent relation to its invasiveness, as indicated by the frequency with which it is found in positive blood cultures. The high mortality in cases of pneumonia of the higher types is considered to be the result of the host factors, as indicated by the frequent occurrence of these types in secondary and in atypical pneumonias.

Case fatality rates have been computed for more than 40,000 cases of "typed" pneumococcic pneumonia, in relation to the kind of specific therapy employed. These cases were collected from many sources, including chiefly large hospitals and the pneumonia bureaus of several states. The case fatality rates were computed for each of the pneumococcus types in cases treated with specific serums or sulfonamide compounds, used alone or in combination, and also in a group of cases in which neither of these agents was used.

These data indicate that both serums and sulfonamide compounds are effective. For many of the higher types the specific serums, used alone or in combination with the drugs, were, relatively speaking, as effective as in the accepted types. Clinical results, as indicated by careful observations in successive individual cases, confirm this impression.

Cases of pneumococcic meningitis are frequently caused by strains of the "higher" types. Serum alone is probably of little or no value in treatment of pneumococcic meningitis, regardless of the type of the organism. The reported results in collected series of cases of meningitis indicate that the mortality is the same in cases treated with sulfonamide drugs alone and in those in which antipneumococcus serums are used in addition, as in cases of pneumonia. Such a result indicates merely that the sulfonamide compounds are effective in these conditions. There is good reason for believing that serum was of added benefit in these cases and was probably responsible for many of the recoveries in the cases in which it was used.

It is concluded that antipneumococcic serums of the higher types are effective and that they have a limited field of usefulness in the treatment of cases of pneumococcic pneumonia and meningitis of these types.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

AUSTIN E. SMITH, M.D., Secretary.

DEHYDROCHOLIC ACID (See New and Nonofficial Remedies, 1942, p. 299).

The following dosage form has been accepted.

THE LAKESIDE LABORATORIES, INC., MILWAUKEE.

Tablets Dehydrocholic Acid: 0.25 Gm. (3¾ grains).

SODIUM DEHYDROCHOLATE (See New and Nonofficial Remedies, 1942, p. 301).

The following dosage forms have been accepted:

THE LAKESIDE LABORATORIES, INC., MILWAUKEE.

Ampules Solution of Sodium Dehydrocholate 20% W/V: 10 cc.

Ampules Solution of Sodium Dehydrocholate 20% W/V: 30 cc. vial. Preserved with 0.5 per cent chlorobutanol.

DIETHYLSTILBESTROL (See THE JOURNAL, June 20, 1942, p. 635).

The following dosage forms have been accepted:

ENDO PRODUCTS, INC., RICHMOND HILL, N. Y.

Ampules Diethylstilbestrol, 0.5 mg. per cc. 1 cc. in sesame oil.

Ampules Diethylstilbestrol, 1.0 mg. per cc.: 1 cc. in sesame oil.

Ampules Diethylstilbestrol, 2.0 mg. per cc.: 1 cc. in sesame oil.

Ampules Diethylstilbestrol, 5.0 mg. per cc.: 1 cc. in sesame oil.

THE LAKESIDE LABORATORIES, INC., MILWAUKEE.

Ampules Diethylstilbestrol in Oil, 0.25 mg. per cc.: 1 cc. in sesame oil containing 0.5 per cent chlorobutanol.

Ampules Diethylstilbestrol in Oil, 1.0 mg. per cc.: 1 cc. in sesame oil containing 0.5 per cent chlorobutanol.

Ampules Diethylstilbestrol in Oil, 2.0 mg. per cc.: 1 cc. in sesame oil containing 0.5 per cent chlorobutanol.

Ampules Diethylstilbestrol in Oil, 5.0 mg. per cc.: 1 cc. in sesame oil containing 0.5 per cent chlorobutanol.

Tablets Diethylstilbestrol: 0.25 mg., 0.5 mg., 1.0 mg., 2.0 mg. and 5.0 mg.

NICOTINIC ACID (See New and Nonofficial Remedies, 1942, p. 561).

The following dosage form has been accepted:

PARKE, DAVIS & COMPANY, DETROIT.

Tablets Nicotinic Acid: 50 mg. and 100 mg.

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SATURDAY, DECEMBER 19, 1942

PROBLEMS OF MEDICAL MANPOWER

If there is any one phase of the manpower problem that has been handled from the first with something resembling scientific procedure, it is the utilization of the medical profession. We have always had a reasonably exact inventory of our medical assets. That inventory was made exact before Pearl Harbor. By the President's order a scientifically minded agency was established to distribute these assets properly among Army, Navy, industry and the civilian population. They recognized the need of the armed forces for a definite number of young, well qualified men. They recognized the desirability that industry be supplied with physicans trained in industrial medicine. They realized, indeed, that an expanded, speeded up industry would require more men than were available and secured the cooperation of all volunteer medical agencies in attaining that objective by training additional men. They established a quota for the present of one physician to fifteen hundred civilian population, although we could go on to one to three thousand in many areas without touching prewar levels in those areas. They have realized the need for meeting new demands such as those that prevail in new industrial and munitions areas. For example, only as recently as December 6 the Federation of State Medical Boards of the United States recommended that temporary licenses be provided for the duration of the emergency so that qualified physicians licensed outside the states which now require additional personnel may be brought in to serve the new centers of population. Relocation of physicians to meet new needs is already under way; it should soon be wholly efficient.

The directing board of the Procurement and Assignment Service is doing its utmost to assure the maintenance of a continuing supply of physicians of a standard equal to that supplied in the past—and that has been the highest of any nation in the world. More than twenty-eight thousand physicians volunteered and gave their services without fee of any kind to the Selective Service Boards. More than forty thousand physicians gave up their careers in civilian medical practice to serve with the armed forces. The directing board of the Procurement and Assignment Service for Physicians, its corps area representatives, its consultant committees, its state and county representatives, some hundreds in all, serve without one cent of remuneration. The hundreds of physicians on the consultant committees of the Division of Medical Sciences of the National Research Council and on the Office of Scientific Research and Development serve day after day at considerable sacrifice of time and income without one cent of remuneration. Throughout the nation thousands of doctors give of their time and effort in the agencies devoted to civilian defense, certifying the young and the old and the sick and disabled for extra fuel, gasoline and rationing of foods, and this service too without remuneration. Can any other profession or trade match this remarkable record of self sacrifice?

Yet they have not had even the appreciation that is their due. Just recently the *Saturday Evening Post* carried a half baked, incompetent, incomplete article on the shortage of doctors, apparently exalting the manner in which Great Britain has handled the problem. Neither the British nor the American situations are presented adequately. The press has carried the news of the attempts that have been made to toss the utilization of American medicine for the emergency into the arena of political football. Striving for political advantages, assaults have been made publicly on the motives, even the integrity, of the Procurement and Assignment Service and of the physicians who participate in its efforts. Fortunately for the American people, those efforts seem now to have failed. Serene in the confidence of the humanitarian, idealistic unselfishness of their work, they go forward even now planning scientifically to maintain for the armed forces and the people of America during 1943 and even during 1944 and 1945, if that should be necessary, a maximum personnel of high quality in the field of medicine, assuring to the people the best that medical science has achieved to keep them free from the fears of sickness, pain, disease and death.

IMMUNITY AND PROTEIN RESERVES

According to a recent presidential address before the American Association of Immunologists by Dr. Paul R. Cannon [1] the last two decades have seen the general acceptance of a new theory of specific antibody production with numerous practical applications to nutritional physiology in wartime.

Toward the close of the nineteenth century the accepted theory of specific immunity was based on Ehrlich's specific receptor hypothesis. This assumes that specific antibodies preexist as hereditary "receptors" or "side chains" in fixed tissue cells, from which they are given off as a result of contact with corresponding specific antigens. Accumulated clinical and experimental evidence eventually led to an almost unanimous discarding of this theory in favor of the concept that protective antibodies are newly formed chemical complexes, synthesized as a result of the action of normal intracellular enzymes.[2] Antibodies were conceived to be acquired chemical characters, whose method of synthesis became a feasible problem in biochemical research.

Numerous biochemists became interested in this basic problem. Breinl and Haurowitz [3] of Czechoslovakia, for example, studied in vitro reactions between purified alien hemoglobin and rabbit precipitin. Analyses of the resulting precipitates by colorimetric, chemical and enzymic methods brought the conclusion that the precipitating antibody is chemically identical with normal rabbit serum globulin except for the spatial arrangement of its constituent amino acids. From this it seemed evident that specific precipitins are normal serum globulins whose intracellular synthesis is modified by the "templating" action of the absorbed antigen. The locally synthesized "antigenic template" thus replaced the hereditary "cell receptor" of the earlier theory.

In his presidential address Cannon reviewed the accumulated experimental evidence in support of the "template" theory, with additional evidence suggesting that the "antigenic template" is synthesized from the intracellular protein reserves. Luck [4] and others showed that a high protein diet leads to an increase in fixed tissue protein reserves with parallel increases in circulating serum globulin. A diminution in cytoplasm protein associated with decreased serum globulin as a result of low protein diets was demonstrated by Elman and Heifetz.[5] These facts suggest the probable importance of a luxury protein diet for the maintenance of adequate "antibody matrix" (protein reserves) to serve as basic materials for specific antibody templation. If so the immunologic potential of the reticuloendothelial system, for example, would vary quantitatively with the amount of locally available protein reserve.

This suggested relationship is in line with statistical evidence covering the increased susceptibility to infectious diseases observed as a result of dietary insufficiency during the first world war. Cannon was able to confirm this relationship on experimental animals. Rabbits whose protein reserves had been reduced by low protein diets showed a distinctly subnormal capacity to produce specific antibodies.

The accumulated evidence in support of the relationship between protein reserves and specific immunity is of particular interest at present in view of the popular overemphasis of the role of vitamins in promoting antimicrobic resistance. There is a resulting popular underestimate of the basic importance of a luxury protein intake. Without more than enough protein to maintain nitrogenous equilibrium, antimicrobic vitamins are immunologically ineffective. In the words of Madden and Whipple,[6] "The reserve store (of protein) is the bulwark against infection."

1. Cannon, Paul R.: J. Immunol. **44**: 107 (June) 1942.
2. Manwaring, W. H.: J. Immunol. **12**: 177 (Sept.) 1926.
3. Breinl, F., and Haurowitz, F.: Ztschr. f. physiol. Chem. **192**: 45, 1930.
4. Luck, J. M.: J. Biol. Chem. **115**: 491 (Sept.) 1936.
5. Elman, Robert, and Heifetz, C. J.: J. Exper. Med. **73**: 417 (March) 1941.
6. Madden, S. C., and Whipple, G. H.: Physiol. Rev. **20**: 194 (April) 1940.

SEASICKNESS AND AIRSICKNESS

About 40 per cent of any population group, Schwab [1] points out, are susceptible to seasickness on sudden exposure to rough weather at sea. About 5 per cent of such a group are subject to intractable seasickness. Rough estimates are that between 0.25 and 0.5 per cent of sea going people are afflicted with chronic seasickness. During wartime conditions when complete cooperation of all sea going personnel is often required, the percentage and seriousness of seasickness may affect the efficiency of handling both merchant and combat vessels. Schwab says that chronic seasickness in naval personnel may be divided into two groups: those who are constitutionally sick with a history of car, bus and other sickness, whose efficiency at sea is extremely low, and those who have severe seasickness without the history of other sicknesses on shore and with a fair degree of efficiency at sea. He suggests that those in the first group are not useful afloat and might be either discharged from the Navy or placed on shore duty. Those in the second group tend to improve with time or treatment or with transfer to larger ships. Gastrointestinal abnormalities were found in over half of the whole group. Schwab did not find correlation with background, race or body type in either of these forms of seasickness. Persons falling in the first group may be readily identified, he claims, by the use of a simple questionnaire.

A related problem of possibly even greater urgency is airsickness. Airsickness is a syndrome which

1. Schwab, R. S.: Chronic Seasickness: Neurological, Psychiatric and Naval Aspects, U. S. Nav. M. Bull. **40**: 923 (Oct.) 1942.

includes sweating, pallor, nausea and vomiting. These symptoms occur primarily while the person is in the air, but cases have developed after the flight has been completed. Flaherty [2] reports that airsickness is frequently found among student pilots and usually occurs during the phase of training in acrobatics. If not properly treated, airsickness may be the cause of failure in making satisfactory progress in flight training. There is, he says, a close neurologic relationship between the vestibular apparatus and the eye. Airsickness is due to poor orientation in space. It can ordinarily be overcome when a student becomes oriented in the air by using his eyes to pick up points of reference on the ground.

Flaherty proposes a program to aid in ocular orientation. The program includes adjustment of the seat, tightening the safety belt, keeping the eyes out of the cockpit and on a distant object, and avoidance of repetition of a maneuver. During a ten months period he treated an average of eighteen students a month for airsickness by this means with satisfactory results. Five students were dropped from flight training because of airsickness, only one of whom was treated according to the advised method. This one had a record of previous car sickness, train sickness and swing sickness, and his training was discontinued prior to the acrobatic stage.

CONSTITUTIONAL EFFECTS OF DYSENTERY TOXIN

A long discarded clinical theory is revived as a result of studies of the systemic action of dysentery toxin recently reported by Penner and Bernheim [1] of Mount Sinai Hospital, New York. A century ago Sydenham,[2] Conradi [3] and others assumed that dysentery is a constitutional disease of which the colonic manifestations are but relatively unimportant secondary features. With the introduction of modern bacteriologic methods, however, dysentery came to be viewed as a strictly local disease due to the direct action of the dysentery bacillus on the intestinal wall. The constitutional symptoms of the disease were ignored except as possible consequences of the local microbic lesion. Doubt as to the validity of this interpretation was expressed by pathologists, who called attention to the clinical evidence that a period of toxemia precedes the onset of the intestinal symptoms by several days and frequently persists for some time after.

From the point of view of the pathologic anatomists, bacillary dysentery is a diphtheritic, ulcerative process similar to the lesions that may occur as a result of homeostatic responses to various shocklike conditions. In studying necropsy material from 47 cases of toxic or postoperative ulcerative and diphtheritic enteritis, Penner and his colleagues were impressed with the association of all their cases with shocklike conditions and with the fact that all of the earliest anatomic changes were in the submucosa. They traced the successive vascular events leading to the ultimate necrosis of the epithelium and concluded that the vasomotor mechanisms which occur in shock are responsible for the terminal lesion.[4] This conclusion was confirmed by the production of a similar chain of vascular events leading to digestive tract ulceration in laboratory animals by repeated daily intraperitoneal injections of epinephrine.

To test the possibility of a similar vasoconstriction production of the colonic lesions of bacillary dysentery, Shiga toxin was prepared by the "slow method" of Olitsky and Kligler.[5] The potency of this toxin was such that 0.25 cc. per kilogram injected intravenously killed rabbits within forty-eight hours. In the initial experiments this toxin was injected intravenously in doses of 0.5 cc. per kilogram into dogs, control injections being made with sterile broth or with heat inactivated Shiga toxin. The toxin injection was followed by shocklike symptoms, which persisted for about eighteen hours and were followed by a gradual return to normal. Blood examinations made at fifteen to thirty minute intervals during this shock showed a significant rise in hemoglobin, erythrocyte count, hematocrit reading and specific gravity of the whole blood, the specific gravity of the blood plasma, however, remaining unchanged. These results indicate that the Shiga toxin produces typical shocklike hemoconcentration.

A compensating vasoconstriction in the duodenum was demonstrated by killing dogs seven to eleven minutes after the toxin injection. The dogs were killed by an intravenous injection of solution of formaldehyde. The digestive tracts of these and an equal number of control animals were opened and immersed in an acidified saturated solution of amphetamine containing a small amount of hydrogen peroxide. The amphetamine solution produces a deep blue on contact with the red blood cells in the intestinal mucosa. The toxic dogs showed focal blue staining areas of the duodenal mucosa, as contrasted with the diffuse staining in the control animals. Penner interprets this as evidence of focal mucosal vasoconstrictions, compensating for the evidently decreased circulating blood volume. Somewhat similar mucosal vasoconstrictions were noted in rabbits, in which animals, however, the vascular reaction is largely confined to the cecum.

2. Flaherty, T. T.: Airsickness During Acrobatics, U. S. Nav. M. Bull. **40**: 902 (Oct.) 1942.

1. Penner, Abraham, and Bernheim, Alice Ida: J. Exper. Med. **76**: 271 (Sept.) 1942.

2. Cited by Latham, R. G.: The Works of Thomas Sydenham, London, Sydenham Society, 1848, pp. 169-170.

3. Cited by Woodward, J. J.: The Medical and Surgical History of the War of the Rebellion, Washington, D. C., Government Printing Office, 1879, part 2, p. 1.

4. Penner, Abraham, and Bernheim, Alice Ida: Acute Postoperative Enterocolitis, Arch. Path. **27**: 966 (June) 1939; Acute Postoperative Esophageal, Gastric and Duodenal Ulceration, ibid. **28**: 129 (Aug.) 1939; Experimental Production of Digestive Tract Ulcerations, J. Exper. Med. **70**: 453 (Nov.) 1939.

5. Olitsky, P. K., and Kligler, I. J.: J. Exper. Med. **31**: 19 (Jan.) 1920.

To test the direct action of Shiga toxin on the mucosa, repeated doses of the toxin were introduced into Thiry-Vella midjejunal intestinal loops. Practically no direct toxic effect was noted in these nonduodenal loops. Absorption through the jejunal mucosa, however, was deduced from the appearance of typical duodenal lesions in the same dogs. From this and other evidence Penner concludes that the pathologic alterations in the intestinal tract following jejunal absorption or intravenous injection of Shiga toxin are the anatomic end results of a pronounced and prolonged homeostatic duodenal vasoconstriction.

Thus far the investigators have not attempted to apply this ancient theory to the treatment of human dysentery. Evidently, however, their systemic theory of the nature of the colonic lesion suggests numerous hitherto untried methods of prophylaxis or therapy.

Current Comment

HEALTH CONDITIONS IN A NEW YORK CITY DISTRICT

A recent review of the health and the social and economic conditions in a small area in East Harlem, New York City,[1] revealed 3,653 instances of chronic disease among 2,863 of 9,119 persons. Nearly 1 out of every 3 persons suffered from one or more specific types of chronic ailment. Some 539 cases, or 5.9 per cent of the studied population, had venereal diseases. The highest incidence, 6.9 per cent, was found among the Puerto Ricans, who constituted 46 per cent of the studied group; the incidence among the Negro and white groups, 37 and 17 per cent of the population respectively, was 6.04 and 2.9 per cent respectively. Some form of cardiovascular disease was found in 5.65 per cent of the surveyed population. Tuberculosis ranked third in prevalence of chronic diseases in the studied population. Indeed, the death rate from tuberculosis of the area in 1939 was three times as high as that for New York City as a whole. The population makeup of the area did not entirely explain the high degree of prevalence of tuberculosis. The high rate of 5.9 per cent was expected for the Puerto Ricans, but the rate of 3.3 per cent for white persons was significantly higher than that estimated for the entire New York City or United States populations. Of the 361 persons who had tuberculous infection, more than one fourth were children under 15 years of age. The incidence of nervous and mental diseases was somewhat higher in this study than that found in the national health survey; the incidence of cancer and other tumors, while not numerous enough to be statistically significant, did not appear to differ from that in the general population; diabetes was reported in only 53 cases and was not statistically significant. In the area surveyed the Puerto Ricans formed the largest as well as the youngest population group. Nevertheless the total incidence of chronic disease was as great among them as among the Negroes or the white persons: they accounted for almost half of all those suffering from chronic disease and were responsible for a disproportionate percentage of the cases of tuberculosis (68.1 per cent) and venereal diseases (53.8 per cent). The social and economic conditions in this population seemed materially worse in all respects than the averages of the population which surrounds it both in the city and in the nation as a whole. This type of study is more valuable in revealing practical opportunities for introducing improvement than are most general surveys which do not clearly delimit the nature of the problems or the interacting social, economic and health factors.

1. Health, Social and Economic Conditions in Health Area 20, East Harlem Health District, Department of Health, New York City, prepared by Special Committee on Health Area 20 of the East Harlem District Health Committee, 158 East 115th Street, New York, 1942.

PHYSIOLOGY OF DELAYED PARACHUTE JUMPS

Certain hiatuses have become apparent in the available knowledge concerning the physiologic effects of free fall through the air. Additional information on this subject is now supplied by the report of an important investigation of the subject by Carlson, Ivy and their colleagues.[1] Their observations, all made on Mr. Arthur H. Starnes, an experienced parachute jumper, involved careful recordings of physiologic and psychologic elements involved in free falls. Various specially devised or adapted instruments were employed, including a pneumograph-barograph, a voice transmitter, a motion picture camera and an altimeter. Six free falls were studied. These occurred through distances which ranged from 8,400 to 29,300 feet. The rate of free fall varied from an average of 112 to 158 miles an hour in the case of the lower altitudes to 171 miles an hour in the free fall from 31,400 feet above sea level. The rate of fall, they say, depends on the weight of the falling body in relation to the air resistance, which in turn depends on the density of the air and the position of the body. The maximum average rate calculated for 4.6 second intervals was about 229 miles an hour. The heart rate during the free fall from 31,400 feet was within the normal range; this was determined by broadcast to the ground by special apparatus which picked up cardiac potentials from chest leads. The blood pressure is not significantly influenced, according to the evidence based on Mr. Starnes's reactions during fall and on studies carried out during rapid recompression in an altitude chamber. A transient "blackout," or loss of consciousness, may occur when the rate of fall is suddenly checked by the opening of the parachute. Respiration is irregular, varying from three to fourteen respirations during the various free falls. Auditory acuity is definitely diminished during free falls; visual acuity, however, is not impaired when goggles are worn. The position of the body during a free fall is not fixed, and the body tends to wobble, twist and spin. However, the human body can be kept nearly vertical, with head up and without vertical spinning, by use of an accessory "antispin" parachute. This position has certain physiologic advantages and reduces

1. Carlson, A. J.; Ivy, A. C.; Krasno, L. R., and Andrews, A. H.: The Physiology of Free Fall Through the Air: Delayed Parachute Jumps, Quart. Bull. Northwestern Univ. M. School **16**: 254 (Winter Quarter) 1942.

one of the hazards of parachute jumping, namely twisting and fouling of the shroud lines of a parachute. Convincing evidence was obtained that, at least in the experienced person, mental reactions are clear and rapid during an extended free fall through the air. Of the various positions of the body in falling the rapid, flat spin, according to Mr. Starnes, is the most uncomfortable and the most difficult to break by voluntary movements. Falling feet down at an angle of about 75 degrees, so that one can view the earth, is the most comfortable. The principal conclusion agrees with that previously expressed by Lieut. Col. H. G. Armstrong,[2] namely that delayed parachute jumps are an entirely practical means of avoiding certain highly hazardous aerial situations, such as the danger of the parachutist being shot down by an unscrupulous enemy in a plane.

THE WAR SURGEON

There is no substitute for the artistry and technic of a competent surgeon. Technics change. New drugs and new operative procedures may greatly improve the results of surgery but the most important factor in the treatment of war wounds, as was said by an anonymous writer in World War I, is the good surgeon. In *War Medicine*, published by the American Red Cross Society in France for the medical officers of the American Expeditionary Force, appeared a statement, unsigned but believed to have been written by J. M. T. Finney in 1917, which emphasizes the fact that the surgeon himself is the most important factor in surgical care:

"By sound surgery we mean the assumption of complete inclusive responsibility for every item that enters into the result; the consideration of the wound as well as the patient; the development of an ability to read the wound as well as the man aright. It means quick, innocuous, timely intervention; it means seeing clearly the tomorrow of the wound; it means no intervention unless there is to be a net gain; it means a sharp knife, a good anesthetic, a painless innocuous dressing; it means as much respect for the tissues of the anesthetized man as for the unanesthetized man; it means a training in judgment that unerringly tells when to cut, how far to cut, when to quit cutting. It plays all the defenses and reparative forces of the patient. Good surgery is the exponent of no single method. It recognizes the anatomical and environmental situation in which chemical and physical agencies are useful. Good surgery exploits physiologic rest and fluids and sleep; gives little pain. Good surgery evokes confidence; and confidence begets rest; and rest begets restoration. Good surgery, then, makes use of antiseptics and physical forces, just as it uses incisions, counterdrainage, revisions, skin grafting, blood transfusion. Good surgery does not substitute an easy formula for its principles; above all, it always is dissatisfied with its work and is open to suggestion.

"What can the good surgeon accomplish in war with wounds, with good opportunity but no antiseptics? Without antiseptics he can close by primary union a higher percentage of contaminated wounds than he can with antiseptics; he is able to remove damaged tissue with such accuracy that the natural defenses of the revised wound become its best antiseptic; he closes penetrated knee joints more securely without than with antiseptics; he closes penetrated skulls without, better than with, antiseptics; he operates on perforated intestines more successfully without than with antiseptics; he clears up foul and infected superficial wounds as well without as with antiseptics; he meets gas gangrene with the timely use of the knife as well without as with chemical agents. He closes healthy superficial wounds with early suture tied lightly; healthy wounds that cannot be closed by suture he closes by skin grafting, both as a healing and as a bactericidal policy; he closes fecal and urinary fistulae without antiseptics. . . .

"In the rush of a great battle, he would incise for drainage, and in addition he would make 'physiologic incisions' to avoid tension that is sure to follow the next day from the inevitable infection.

"But in quiet times he would dissect out with macroscopic exactness every atom of devitalized tissue. He reads accurately not only the wound but the patient, not only the patient but the military situation, not only the military situation but the condition of the infecting soil, the state of transport, his surgical assistance and the type of nursing care—that is, he weighs accurately his chances for success. Therefore the army medical service and the wounded man pin their hope and their faith first, last and always to the one agency of wound treatment that in civilian surgery emerged clearly from the confusion of the listerian period, is emerging clearly from the confusion of the four years of military surgery—the sane, sound surgeon."

BRITISH MEDICAL PLANNING

Further light on the attitude of the British Medical Association to the now famous Interim Report of the Medical Planning Commission is given by the votes on two resolutions that were brought up in the discussion of this report at the annual representative meeting of the British Medical Association.[1] A motion with regard to medical service "that provision, of whatever character, should be made by the government for the whole community" was, after considerable discussion, adopted by the very close vote of 94 for and 92 against. The effect of this was also immediately modified by the adoption of a "rider" providing that "the patient should have the right to contract out and the doctor the right to charge fees for attendance to patients not on his list." A motion "that the basis for the coordination and integration of health services should be the establishment of a whole time salaried government service" was defeated by a vote of 20 to 177. This would apparently indicate an overwhelming opposition of the medical profession to a comprehensive state medical service.

2. Armstrong, H. G.: Subjective Mental and Physical Reactions to a Free Fall in Space, J. A. M. A. **105**: 1107 (Oct. 5) 1935.

1. Brit. M. J. supplement, Sept. 26, 1942, p. 33.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war and such other information and announcements as will be useful to the medical profession.

CIVILIAN DEFENSE

PROTECTION FOR INDUSTRIAL PLANTS

The Office of Civilian Defense, Washington, D. C., has published a pamphlet entitled "Passive Protection for Industrial Plants" in which, in the section on "Medical Services," it is recommended that each industrial plant, in addition to providing its own medical staff and first aid equipment, should plan in collaboration with the chief of the Emergency Medical Services of the locality for (1) services of ambulances and Emergency Medical Field Units when needed, (2) available beds at one or more hospitals to which the severe casualties may be transported, (3) the establishment of a casualty station of the Emergency Medical Service within a short distance of the plant and (4) obtaining the services of Emergency Medical Field Units if needed to supplement the plant medical service during an emergency.

If the industrial plant is miles from the hospital, the casualty station should be larger than the average and must be equipped at least with the emergency medical supplies in medical division bulletin No. 2, equipment lists 1 and 2. The primary purpose of the casualty station is to care for the slightly injured and thus protect the hospitals from caring for minor casualties; it will serve also as a center for the storage of medical supplies and for the dispatch of medical service to different parts of the plant. The first aid posts are established at the time of emergency as near as possible to where the casualties are being extricated.

All general hospitals in the community are included in the Emergency Medical Service, and the community control center will designate the hospital to which casualties from the industrial plant may be sent. Trained stretcher bearer teams should be organized among the employees by the medical director, each team comprising four persons. Five per cent of the plant personnel should be trained in these duties in order to have stretcher teams on call during each shift and in each wing of the plant. The minimum number of stretchers recommended, according to this pamphlet, is in plants having from one to ninety-nine employees—one stretcher for each twenty-five persons, and in plants having from one hundred to four hundred and ninety-nine employees, one stretcher for each fifty persons (minimum of four).

It will be advisable for industrial plants to provide improvised ambulances for their use in the event of an emergency. All requests for ambulance service from the community should be made to the control center of the Citizens' Defense Corps.

CHANGE IN TERMINOLOGY OF CIVILIAN DEFENSE DIRECTIVES

In view of the revised system of directives of the Office of Civilian Defense, Washington, D. C., established by operations letter 83, the previous series of Medical Division memorandum will end with No. 18. The Medical Division Memoranda series will be continued as Circular, Medical Series, and will be numbered consecutively, beginning with No. 19, dated Nov. 10, 1942, in which the foregoing information is contained.

CIVILIAN DEFENSE PERSONALS

Dr. M. V. Ziegler, formerly director of Division No. 3 of the U. S. Public Health Service, has left Chicago to become regional medical director of the Office of Civilian Defense in Baltimore.

MISCELLANEOUS

PUBLIC HEALTH UNDER HITLER

According to DNB of September 17, doctors from twenty-five countries have assembled in Innsbruck for a conference of foreign and German doctors. In addition to the friendly European countries, Japan, China, India and Thailand are represented. The conference, which is under the patronage of Gauleiter Hofer, has been jointly arranged by the foreign department of the reich health directorate and the foreign department of the Union of University Teachers. The discussions are concerned above all with the question of preventive medicine, cancer research and the fight against cancer, population policy and tuberculosis.

Reich leader of university teachers Dr. Schultze declared that this conference of German and foreign doctors lasting for a week in the midst of war provides proof of Germany's strength in the scientific and cultural spheres and shows how a European way of thinking and feeling is increasingly taking shape. Reich health leader Dr. Conti in the chief speech of the day outlined the health situation of the German people. A people can prosper only if it has sufficient space and sufficient soil for cultivation; otherwise a pathologic development is inevitable. We Germans were today fighting for the soil which we need to live.

Dr. Conti dwelt with emphasis on the idea of racial welfare (rassenpflege), which has often led to misconceptions and even to malicious interpretations abroad. The idea of the value of blood is not a factor which separates nations but one which reconciles them by the recognition of natural differences.

According to NDZ of September 16, the reich minister of the interior has issued a decree aiming to provide adequate dental services for the population of the reich. The decree authorizes the reich leader of dentists to direct dentists to settle in districts where there is no provision for the dental needs of the population. On the other hand, a dentist may not close his practice without having previously obtained permission. The minister of the interior has been authorized to reform the training of dentists so as to make it uniform throughout the reich.

According to NDZ of September 22, in order to unify the measure of preventive and protective care for infants and toddlers in all advice bureaus for mother and child, infant welfare centers and similar institutions, Dr. Conti has made it compulsory to keep "health record sheets for the infant and toddler," which will be uniform for the whole reich. All state, communal and party authorities must in future use those health record sheets. These will register the child's development, cases of illness, condition of the teeth, prophylactic treatment for rickets and other items. The health record sheet is protected by the pledge of secrecy customary among the medical profession, which is extended to all those engaged in preventive and protective care of infants. The sheet is to be kept in the health office, or in the advice bureau of the health office or the NSV of the district in which the child resides. As the child grows older the health record sheet for infants and toddlers will serve as a basis for the new health record sheet for juveniles, which it resembles.

NDZ of September 21 publishes extracts from an article by Oberstabsarzt Dr. Ruhe in the periodical *Gesundheitsführung* dealing with the special measures of medical care, retraining for civilian life and the like for seriously wounded soldiers.

There are special military hospitals for blinded soldiers and for men with brain injuries where the men are given a certain amount of training under medical supervision to fit them once more for civilian occupations.

Krakauer Zeitung of September 6 reports that the German minister of health, Dr. Conti, accompanied by Oberfeldarzt Dr. Bernhardt, arrived in Warsaw on September 5 for a short visit. He spoke with medical personnel and military surgeons.

According to *NDZ* of September 12, virulent epidemics no longer threaten the life of the nation, even in times of war. Tuberculosis, however, has by no means been deprived of its terrors. The first world war with its increase of tuberculosis has given much food for thought. In order to prevent similar developments from the start and still further to improve combative measures, the ministerial council for the defense of the reich has issued a decree regarding tuberculosis assistance by the reich. The reich health leader, Dr. Conti, discusses the contents and significance of the new measures in the *Völkischer Beobachter*. To the old age pension scheme, which provides for every insured German, the decree adds tuberculosis assistance for every one who has contracted tuberculosis, with services which will prove adequate and successful for preventing epidemics. It provides for treatment of the sick person up to the time when he regains his health or is able to resume his work without fear of infecting other people. It provides for continued supervision of his state of health and also cares for the family of the sick person, whose economic distress has so often in the past induced the patient not to undergo the necessary sanatorium treatment. Fundamentally new is the provision that clinical treatment in a hospital for tuberculosis or a sanatorium is granted immediately for purposes of observation and reliable assessment of the chances of recovery. Social insurance and tuberculosis assistance by the reich will thus in future be the main pillars supporting the fight against tuberculosis. There are at present thirteen hundred tuberculosis advice centers of the health offices in full operation. Over one million seven hundred thousand x-ray examinations have been made and two hundred forty thousand x-ray photographs have been taken in the centers. Over six million people have been examined since the outbreak of war by the x-ray section (sturmbann) of the S. S. Thousands of previously unknown cases were thus diagnosed. A certain increase in cases of tuberculosis will be unavoidable even in this war. The decree, however, even at this stage, creates the organization and financial foundations for a successful fight against tuberculosis. We have made certain that tuberculosis will not threaten national health during the war.

DNB of September 12 adds the following details: Under the new decree welfare societies and regional welfare associations will be created which will grant tuberculosis assistance to the rural and town population on the application of the health offices and in collaboration with them. On principle tuberculosis assistance is free of charge; it includes treatment, isolation and medical care as well as economic support for the patient and his family. The welfare associations grant tuberculosis assistance if the taxable annual income of the patient does not exceed 7,200 reichsmarks and unless the necessary assistance is granted by a social insurance institute or in some other way. The limit is raised by 1,200 reichsmarks for a married couple and by 600 reichsmarks for every additional member of the family. Tuberculosis assistance may, however, also be granted if the taxable annual income of the patient exceeds this limit, if there is a danger of the necessary measures not being carried out without assistance. In such cases the welfare associations and the recipients of tuberculosis assistance may, in accordance with the civil code, demand a proportionate refund of the relative expenses from the persons responsible for the patient's upkeep. The decree is to become law after a transitional period fixed by the reich ministry of the interior.

According to the *Deutsche medizinische Wochenschrift* (Leipzig) of July 10, in an article by Oberst Maier in the *Vierteljahrschrift Schweizer Sanitätsoffiziere*, 1941, number 3, it is said that medical examiners have made too much allowance in cases of mental diseases when examining recruits for the army. Psychopaths, sexual perverts, hysterical people, schizophrenics and maniacs, as well as persons with epilepsy and early recognized paralysis may all be accepted if they are put in appropriate posts and can be controlled and led by their superiors.

The *Deutsche medizinische Wochenschrift* (Leipzig) of July 10 contains a review of an article by professor Staub in the *Vierteljahrschrift Schweizer Sanitätsoffiziere*, 1941, number 3, on the influence of drugs on mental and physical performance. He asserts that, in contrast to the first world war, the consumption of alcohol has been found not to promote the capacity for military operations but to be definitely detrimental. Amphetamine and pervitin (a synthetic amine chemically related to ephedrine) are indicated when a single special performance is wanted. There must, however, be a corresponding training and adequate nutrition. In the view of the writer these two drugs are a necessity for motorized troops, as they increase the performance and faculty of observation, while the monotony of driving and the loud noise tire the men and make them sleepy. It would be difficult to imagine a long distance night flight without these two drugs.

DR. MORRIS ON MEDICAL MISSION FROM AUSTRALIA

Dr. John N. Morris, a distinguished Australian physician, is now on a special mission to the United States in the interests of the Australian Central Medical Coordination Committee and the Australian Red Cross. His mission concerns medical supplies and equipment, the need of certain kinds of which is acute. Since the war began, Australia has increased the output of some medical supplies sufficiently to provide for the different military forces serving there and in other cases has found new sources of certain medicaments.

Surgical dressings, however, present a real difficulty, owing to the shortage of cotton. Australia also desperately needs quinine and other drugs used for the treatment of tropical diseases. Quinine cannot be used at present in Australia for prophylactic purposes nor for the treatment of any illness except actually established malaria. This situation is aggravated by the extreme shortage of suitable mosquito netting.

The Central Medical Coordination Committee has formed a Medical Equipment Control Committee, which ascertains the stocks of drugs and medical equipment available, and the National Health and Medical Research Council of Australia has contributed to research work carried out mostly in the universities of Sydney and Melbourne toward the production of new local sources of drugs and biologic products. Dr. Morris points out that Australia has done a fine job solving many of these problems but that they need help. He has come to this country to give us the facts and to acquaint the medical profession of America with the situation in Australia. Dr. Morris is a member of the Australian National Health and Medical Research Council, chairman of the Victoria Red Cross, vice president of the Victory Society for Crippled Children, a major in the Australian Army Medical Corps Reserve, was the first president of the famous Australian Aerial Medical Services and was for many years chairman of the council and formerly president of the Victoria British Medical Association.

RUSSIAN WAR RELIEF

During the first year of operations of Russian War Relief, Inc., the shipments to Russia and goods being purchased reached a total value of $4,067,703.91. Edward C. Carter, president of Russian War Relief, announced on November 12 that supplies are being regularly sent to Russia in Soviet ships at no cost to Russian War Relief, which spends all its relief funds for American products and sends no money to Russia. The total of contributions to this effort to help wounded Russian soldiers and orphans and refugees in the Soviet Union is increasing each month and the supplies shipped are reaching their destination; 90.4 per cent of the supplies have been medical supplies, 6 per cent clothing, knit goods and blankets, 3.5 per cent foodstuffs and seeds, and one tenth of 1 per cent miscellaneous items. The head of the Russian Red Cross, Sergei Klesnikov, and Prof. Sergei Spassokukotsky, Soviet surgeon, recently cabled their gratitude to the American public and Russian War Relief.

ORGANIZATION SECTION

OFFICIAL NOTES

ANNUAL CONFERENCE OF SECRETARIES AND EDITORS OF CONSTITUENT STATE MEDICAL ASSOCIATIONS

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MEDICAL SERVICE PLANS OF THE FARM SECURITY ADMINISTRATION

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The medical care plan is only a part of the general program of the Farm Security Administration which was started in 1935 with the announced purpose of "helping low-income farmers to get a greater degree of independence and security." This general program is based on a system of federal loans accompanied by assistance in farm management and in the organization of local resources. Because the defaults in payment of such loans are alleged to have been due in large part to illness in the borrower's family, the Farm Security Administration introduced a program to provide medical service for its clients.

The first plans were started with little consultation with organized medicine and varied widely in many of their features. A few were legal corporations, some were "farmer cooperatives" dealing with medical societies and occasionally with salaried physicians. Sometimes loans were issued to individual families to pay for specific services with little group organization. Contracts were, in some localities, made with groups of physicians. This diversity involves no criticism. Given the existing state of knowledge or, better, ignorance of the factors involved in the problem of organizing any general plan of providing medical service, it is necessary to proceed by "trial and error" with a certainty that there will be no lack of either "trials" or "errors" by those conducting the experiment.

These experiments did demonstrate that any successful plan of medical care must rest on constant consultation and close cooperation with the physicians who give that care and with the medical societies which alone represent the medical profession.

The Farm Security Administration has now adopted a policy of close cooperation with state and county medical societies and is pledged not to introduce any plan against the opposition of such medical societies. The 1940 report of the administrator of the Farm Security Administration says (Report of the Administrator of the FSA, 1940, p. 91):

> The entire program has been worked out in close cooperation with the state medical associations and local medical societies. Before a medical plan is set up in any state a memorandum of understanding is drawn up by the Farm Security Administration representatives and the state medical association.

Any agreement for medical services must be satisfactory to the state and county medical society as well as to the Farm Security Administration and usually provides for termination if conditions unsatisfactory to either side develop. The present tendency seems to be to confide financial administration to a "farm cooperative," managed by the farmers but having no functions concerned with medical service.

The state and county medical societies to which this program has been presented have, with a number of exceptions, generally agreed that the income classes included in these plans were not previously receiving proper medical care and were at least partially dependent, and also that the physicians who had cared for them in the past received little for the services supplied.

On June 30, 1942 there were 793 units of the medical plan operating in forty states covering 1,017 counties and having a membership of 109,964 families including 578,804 persons. More than half of the persons served (316,925) are in the five states of Alabama, Arkansas, Georgia, Pennsylvania and Florida. The Agricultural Workers' Health and Medical Association of California provided medical care for an additional 54,989 persons in 1941 and has expended about $5,000,000 in provisions for transient laborers since March 1938, of which nearly $4,000,000 was for medical care.

A request addressed to the secretaries of state medical societies in which Farm Security Administration medical plans exist brought much information of value in arriving at conclusions as to the professional point of view. In general, the answers to the question as to the attitude of the profession brought a vote of nearly 4 to 1 on the satisfactory side. The states reporting lack of satisfaction were almost invariably those whose experience with such plans was confined largely to the earlier and more experimental stages. Criticisms were more frequently made in localities where economic conditions did not indicate a need for any special plan. Twenty-one out of twenty-eight states reported that the families included were receiving more or better or at least earlier medical care than they had received before introduction of the plan. There was almost equal unanimity of opinion that the physicians as a whole received more money under the Farm Security Administration plan than they had been able to collect from the same body of patients previously. It must be remembered that these plans were started in the depth of the depression when physicians in these localities were granting services to a large body of farmers who were at that time unable to pay much for it. Also that the loans granted to clients for medical services were very inadequate. The opinion is also expressed that better economic conditions have rendered such plans less necessary. In the first plans loans of as low as $14 to $20 per family annually were common, and the total sum was distributed on a "unit system" with basic fees sometimes amounting to only 50 or 60 per cent or even less of the prevailing fee schedule. Later plans increased this payment, but there are still many complaints of insufficient pay. Two excuses have been offered for such insufficient payment: (1) the appropriations fix a limit and (2) many of these farm families are semi-indigent and would be cared for by physicians with little or no pay. Neither of these explanations can be considered adequate, but any financial differences are subjects for bargaining and adjustment.

There was in the beginning a lack of any clear definition of the medical care to be given and an absence of any competent and authoritative professional agency to decide disputes as to such limits. There have been some complaints of an excessive demand for medical services shortly after plans have been established, especially for preexisting conditions, while, on the other hand, some medical societies comment on the cooperation of the patients in restricting their demands to actual need. This would seem to call for advice to clients by the administration based on simple but ample explanation of just what services can be given.

A recent development holds far wider possibilities. The Farm Security Administration, as an agency of the Department of Agriculture, in cooperation with the Interbureau Coordinating Committee on Postwar Programs, is undertaking an experimental program to provide medical care to farm families without fixing any definite income limits. This program is being conducted through state and county agricultural planning com-

mittees, which are extensively organized throughout the United States. It is easily possible that this plan may expand to include a major part of the entire farm population.

The experimental character of this program and the necessity of close cooperation with the professional associations is repeatedly stressed in the material issued by the Interbureau Coordinating Committee. It is recognized that the extent of the medical care to be given must be somewhat limited but that "the first consideration" in any plan for medical care must always be "the quality of the service" and also that "the high standards already set by certain prepayment medical care plans developed or sponsored by the medical profession can serve as guides in the development of local plans." The further policy is declared that "all strictly medical aspects of the program should be left to the professional groups concerned, while matters of business management will ordinarily be the responsibility of the farmers' organization."

State and county medical societies have done much to improve and perfect the Farm Security Administration plans. Extensive and costly surveys have helped to eliminate defects and insure better medical care. More accurate and intelligible limitations and descriptions of the medical services susceptible of being given for the funds available have been developed. This is the basic point of every prepayment plan. It is doubtful if any plan, public or private, has ever given a fully "complete medical service." The problem is to determine just what is possible with the available resources and then to be sure that the public to be served understands fully just what can be given. Nearly all private and governmental prepayment schemes, and especially those given most publicity, are consciously or unconsciously guilty of deceiving those who are promised the service.

The medical care provided by these experimental plans, while still limited at several points, is more comprehensive than in the previously existing Farm Security Administration plans, although it is recognized that "complete medical and dental care remains an ideal." The service now proposed includes general practitioner services as a base and, with numerous limitations, specialist, hospital, dental, pharmaceutic and nursing services. In these plans monthly payments are adjusted to approximately 6 per cent of the income with a maximum of between $50 and $60 annually per family varying with the size of the family units. Since 6 per cent of the lower incomes manifestly will not produce the payments necessary to furnish the proposed medical service, a government subsidy is added which in some plans approaches $100,000 annually.

Six of these experimental plans are in operation or in process of organization. Of the plans in operation, one each is located in Texas, Mississippi, Nebraska and Arkansas. Another in Texas and one in Georgia are about to start. The membership of these plans at present varies from 1,000 to 3,000 families. All are operated under agreements with organized medicine much the same as other Farm Security Administration projects.

The Farm Security Administration has expressed its desire to cooperate with prepayment plans operated by state and county medical societies wherever possible and at present is working in cooperation with such plans in California, Oregon and New Jersey and is negotiating with the Western New York plan.

The California Physicians' Service seems to have developed the most comprehensive plan of cooperation with the Farm Security Administration. Because this is based on a longer experience with more phases of the Farm Security Administration program than has existed in most states and therefore possibly forecasts a future stage of evolution, a somewhat fuller description and discussion may be helpful. The California Physicians' Service has established a Rural Service Department to care for all Farm Security Administration clients. The program is planned for statewide coverage of farm families, although it is at present largely confined to a few counties. There is an annual income limit of $2,000.

Annual payments are graduated according to size of the family from $20 for one adult to $60 for a family of three or more. The patient pays $1.50 for the first home call; care for adult chronic cases is limited; surgery for preexisting conditions is excluded, and x-ray and laboratory procedures require special authorization by the medical director of California Physicians' Service. Service is not given for alcoholism, refractions, workmen's compensation cases or conditions for which services are furnished by federal, state or other agencies. Ward service is given in a hospital for twenty-one days while the patient is under the care of a professional member of California Physicians' Service. The cost of hospitalization and medical care in confinement is limited to $25. The first $5 for drugs, which are also somewhat limited, is paid by the patient. No dental care is given.

Dr. A. E. Larsen, secretary and medical director of California Physicians' Service, says in a letter "The Farm Security Administration, the local Farmers' Health Association and individual patients have all expressed their complete satisfaction with the quality of the service." He also says "The physicians are receiving more payment from these families under this plan than was previously received from them." As to the attitude of the medical profession, he concludes "The decision to extend this contract throughout the state and to procure an active campaign of enrolment of additional families was made as a result of complete satisfaction on the part of the medical profession in the state as a whole. The action of the California Physicians' Service board of trustees in entering into this field was approved and commended by the house of delegates of the California Medical Association at their meeting in May of 1942, and further confirmation has been given the Council of the California Medical Association for the extension of this program."

There have been theoretical objections and charges that such plans are a step toward "state medicine," "compulsory sickness insurance" or "socialized medicine." In evaluating such objections, it may be well to consider alternatives. It has become axiomatic that this war will bring great changes in all institutions. News from Britain, Canada, Australia, New Zealand and South Africa reveals almost parallel movements throughout at least the English speaking world in the direction of greater intervention of government in medical care. The introduction of the Elliot bill in Congress, statements of President Roosevelt and the Social Security Board officials, the effort of some hospital insurance plans to invade the field of medical practice and many similar phenomena in a variety of fields are portents of a trend in the United States.

It is doubtful if head on opposition can greatly affect this trend. The House of Delegates of the American Medical Association has laid down the principles which determine its policy. The first of these is the foundation of all the others. It reads: "All features of medical service in any method of medical practice should be under the control of the medical profession." No complaints that this principle is infringed in any Farm Security Administration plan have been reported.

This would seem to be the most general and basic test of the acceptance by the medical profession of any plan of payment for medical service. All other phases may be subject to bargaining and compromise, but any yielding of control of the standards of medical care to those unqualified to exercise that control is a betrayal of the trust which has been confided to the medical profession.

DISCUSSION

DR. GEORGE H. KRESS, San Francisco: The California Physicians' Service is a statewide project under the sponsorship of the California Medical Association. It operates as a separate entity, a separate corporation. Five thousand of our members are professional members of California Physicians' Service. It is now in its third year of operation. It started out with a large number of idealistic, all coverage provisions which almost ran it on the rocks. As time has gone on we have learned that you cannot give all coverage service at these nominal prepayment fees. The Agricultural Health Workers' Association, which took care of the itinerant farmers who came into California, has been put across on a very sound basis, as has been indicated by Mr. Simons. The experience we gained in that project has helped us greatly in connection with our Federal Housing Administration plans and also with the Farm Bureau work. Mr. Simons has indicated the restrictions that have been laid down. Even if these families have only $2,000 annual income, it is mandatory that the first visit be paid, with a price of $1.50 for that first visit. There isn't any doubt but that it will go over in a very large way. The amount of money that has accrued to the physicians is far greater than they ever would have received from these families, because many of the recipients of this medical aid formerly were charity patients. This will undoubtedly run into thousands of dollars, the entire account being kept under a separate heading, separate and distinct from all the other work of the California Physicians' Service. Do not go beyond the sound actuarial basic provisions that are necessary of observance if you want to put your plans across. We learned that to our sorrow in California. We have weathered that storm, and from now on we hope to go on to greater success. Through an extension of these other enterprises in connection with the Federal Housing Administration

and the Farm Bureau Administration, it is possible that California Physicians' Service will be able to put across a program that will be one of the outstanding expressions of medical service to lower income groups in the entire United States.

DR. A. T. MCCORMACK, Louisville, Ky.: We are either going to take care of our farm population or we are going to destroy our civilization. The time has come when, having stabilized our urban centers and our industrial relations to a certain extent and made them independent, they have got to come back and help the farmer. This contribution is an enormous one, and there is a collateral obligation on our part. We not only must maintain the principles which we have established but must gradually realize that there is a difference between the demand for medical service and the need for medical service. Up to the present time, as a profession it has been our practice to respond only to demand for medical service. A man has a pain, he has a fever, he has some symptom and he calls a doctor. The doctor sees that particular patient, who frequently is not the one in the household that needs the most medical attention, and he doesn't see the other members of the family when he is there. The Farm Security Administration is making a notable contribution, and I hope that as soon as they have finished with the great empires of Texas and California and New York they will get to the rural sections of the country where they are absolutely dependent on agriculture, whose whole civilization is based on it, and who realize our obligation to the farmers of our country. We will welcome with open arms in Kentucky the Farm Security Administration when it comes and will promise it complete cooperation, and we will also promise it to do the very best bargaining we can for the benefit of the medical profession.

DR. HOLMAN TAYLOR, Fort Worth, Texas: There is an element of danger in the new developments of the Farm Security Administration medical service concerning which I should like to ask the author. Under the earlier plans—at least down our way—and under an agreement that our council on medical economics made with the Farm Security Administration, there was a measure of protection given the doctor in the matter of medical malpractice damage suits, and with us the doctors were given practical control of the service for which contract was being made, and of the money by which payment was to be made. Down our way the doctors are taking the matter over, and I think you will be told that we are running the medical end of it just as was intended in the beginning that we should do. However, there is now the element of medical malpractice which must be considered.

MR. A. M. SIMONS, Chicago: That is just one of the points that I would say required a good attorney, which I am not, to go into, but it is one of the questions that you can work for. You can say "If this situation regarding malpractice does not protect us, we will not go into it." The ace in the hole that the medical profession holds in every single one of these debates is that nobody has ever found the way yet to give medical service without physicians. That doesn't mean a strike. It simply says that you say "We can't give the sort of medical service we ought to unless we have these protections, and we won't deceive the people." There are certainly dangers in this. There are always dangers in social experiments. We made a lot of mistakes in the prepayment plans, but I think we are coming out ahead. The Farm Security Administration made an unmerciful lot of them in the beginning. Don't say South Dakota to one of them or he will throw something at you for what they did up there, but they are beginning to realize the fact that they need the physicians, and they need the organized physicians—the medical society. Now the question is Are we ready and able to give the information and the help they want? That may not be very satisfactory, Dr. Taylor, but I think the fact is you have to work out all these details always with the one thing in mind that you are not going to let them have control of giving the medical care. There, mind you, is the danger, because you have in your Social Security, in a lot of the social services and in most of your industrial affairs a large part of the medical care.

DR. TAYLOR: In one of the counties that is now trying out this new idea the contract was made by a cooperative group of farmers organized along the financial lines recommended in part with the county medical society itself. That particular society does not happen to be incorporated. If it was incorporated under the laws of our state, it would be a different proposition. But what is the aspect of a cooperative agreement involving a contract with the county medical society and not the individual doctor?

MR. SIMONS: I couldn't answer those questions, but I would say you had better get some good legal opinion on it and find out if you ought to incorporate it.

DR. TAYLOR: The doctors who are going to render this service must be protected against the malpractice laws in our state. We recognized the seriousness of this situation some time ago and undertook to get our legislature to warrant the formation of simple partnerships in counties for the purpose of serving groups of lower income workmen. We didn't get it because of the intervention of the osteopaths. They wanted us to make an insurance problem out of it, and it is not an insurance problem; it is a partnership, a simple partnership for the purpose of taking money however we can get it honestly and honorably and dividing it among ourselves for an honest and honorable service. We failed to get that enabling act through the legislature. If we had that, we could solve that problem of service to the farmer, to the industrialist and to whosoever may be concerned, and we would then be absolved from the damage suits that can come through partnerships.

DR. JOHN HAROLD FITZGIBBON, Portland, Ore.: It has been our impression on the West Coast that a great many of these people from the distressed areas have moved out into war industries. I wonder if any one connected with the Farm Security Administration picture could give us an idea of how many of these people have drifted west and elsewhere into war industries. There must be a tremendous absorption of them, and I should think that would profoundly alter the economic situation in the areas from which they come.

MR. SIMONS: I can say that Dr. Mott and others told me they had studied it somewhat, and they recognize thoroughly, as I mentioned twice in this paper, that changing economic conditions are changing the need. That is a thing we always want to keep in mind. In the ten years I have been with the American Medical Association, the changing economic conditions and the changing source of conditions have changed the picture over and over again. I don't think there is the need for Farm Security Administration help in many of the states that there was.

DR. WILFRID HAUGHEY, Battle Creek, Mich.: I would like to interject one thought. How many farmers are there left in Kentucky and Tennessee? We have had them come into Michigan by the thousands and tens of thousands. One company alone in Michigan is importing 20,000 a month.

DR. MCCORMACK: That is one of the greatest difficulties we have. Whenever there is a boom in Michigan, they come down and induce our innocent people to go up there. They pay them high wages and charge them high prices for living and they get bad habits. Then, just as soon as the bust comes, they hire buses and send them back to Kentucky broke, with the same extravagant habits Michiganders have. Our problem is very much enhanced by having that association.

INTRODUCTION OF GENERAL DAVID GRANT

COLONEL FRED W. RANKIN: One of the outstanding features of the present armed services is the rapid expansion and high efficiency of the Air Corps. It started as a relatively small part of the Army, and today it is certainly one of the dominant forces if not the dominant arm in the whole service. With that expansion the medical forces of the Air Service kept pace, and today I think there is no more outstanding achievement in the Medical Department than the noteworthy efficiency and *esprit de corps* with which medical matters are handled in the air. That this is the fruit of the labors of one man largely, who had the good judgment to surround himself with some very efficient and energetic and alert young officers, I believe there will be small disagreement. That man is General David N. B. Grant, the air surgeon, whom I have the pleasure now to present to you.

MEDICAL PROBLEMS OF THE AIR CORPS

BRIGADIER GENERAL DAVID N. B. GRANT
AIR SURGEON, UNITED STATES ARMY

We have built our service along the plan of first getting *esprit de corps* among our officers and integrating them into the air forces. We have also built our service along the plan of endeavoring to put men into positions in which they are fitted. We have made a hobby of it.

We know we make mistakes, but I was very much gratified that the officers from Jefferson Barracks the other day told me that out of seventy-one officers stationed at Jefferson Barracks less than 1 per cent were not assigned to their specialty. There are a great many jobs in the Army that have to be done, but we are certainly trying to take the outstanding men, putting them in as heads of our services, and stabilizing

those services so they can't be moved, and assuring the men that they are doing the work for which they have been fitted.

We have gone beyond that. I myself feel very strongly, and have for years, as I see this picture unfolding, that the army medical services have a very definite goal to better these doctors for their civil work when they get out. Medicine has become very much specialized, as you know. Aviation medicine covers all the specialties. We feel that with the training we are giving our doctors, whether surgeons, cardiologists or what not, they have a broader picture of medicine when they get out. We also think, this being a global war, that we have got to think in terms of global medicine for the future. The question of tropical diseases in years past has been written into textbooks, as far as I myself know until this time, just to make them a little bit thicker. We have got to know something about that; all the doctors have got to know something about that. We have men today in South America, Africa and, three days later, in Nome.

We also feel that we have an obligation to the public to turn these boys back in better shape than that in which they came to us. We are doing a tremendous amount of salvage work today. Not only are we doing the salvage from the standpoint of operative work, but I am speaking of the morale and the mental side of it. For instance, yesterday orders went out to all our hospitals that there would be started immediately what we call inpatient occupational therapy. All our patients will get some form of instruction, whether it is radio, mathematics or what have you, while in the hospital. The patient will get bed exercises. He may be able to do only finger exercises the first day, but he will graduate up until he gets out of bed. We feel that by doing that we shall return these soldiers to their companies on a duty status, with a little ambition to pick up and go ahead, where they were just standing still before.

We have arranged a form of certification which we send to the company commanders, our estimate of that individual, whether he is interested in radio or what have you. We give them lectures on current events in the wards, moving pictures of something along the military line, which is going to help them. The preliminary estimates in the one hospital where we have tried it show that that has knocked down our sick report—I mean people just coming on sick report—around 25 per cent, and we know we are turning back to the companies better men, not only physically, but mentally.

This is a tremendous war. We cannot afford to lose manpower in any respect. We have taken men with an arm off. The commandant at Kelly Field today is doing one of the best jobs in that line that the air force has had. He has his arm off at the shoulder, which he lost about six weeks ago. In other words, we want to salvage those people and give them an interesting life, and let them know they can carry on. So far, we have been fairly successful.

With reference to the medical societies, all of my hospitals have been instructed to contact the local societies and, if possible, affiliate with them. I hope they are doing it. I think there should be the closest cooperation between military medicine as practiced in the neighborhood and civilian medicine. With the shortage of doctors I think we have got to help one another, and I can assure you from the standpoint of the army air force that help will be forthcoming whenever it is needed or asked for.

MEDICAL SERVICE PLANS

JAMES C. MC CANN, M.D.
President of the Massachusetts Medical Service
Worcester, Mass.

It is probable that if this world change does influence the practice of medicine, and it is difficult for me to think of the millions of boys who are going abroad—many of us may join them within a short time—who are going to contact this undeniable rise of the common man in the rest of the world, who are going to get in personal contact with social institutions and experiments all over this world which are being improvised to meet the demands for security and of economic security and social protection of the common man, it is doubtful if they are going to return and not ask us what we have done so far as fortifying the position of the common man who needs medical care in America. I doubt that he will be satisfied if we say to him "We have given your mother, your father, your brother and your sister adequate medical care as charity." I think that is the crux of the problem.

Of the experiments that have been devised, the prepayment plans of medical care have been looked on as probably the most effective approach, under the auspices of the physician, to solving the problem of the care of the low income group. I am just going to discuss in outline what has been done in building Massachusetts Medical Service. I certainly do not offer it as a sample or plead especially for it, but I offer it as a tree on the branches of which may hang the basic problems with which any group is confronted that endeavors to establish a prepaid medical system for medical care. The answers to these problems I can tell you, having been one of the active members in organizing the Massachusetts plan, are not very easily available; in fact, they are most difficult to get.

The first basic problem is When are the physicians in a state ready to support a prepayment plan of medical care, and how are you going to acquire the support of the profession within the boundaries of the state, because without a list of participating physicians you have no cooperation?

There are various factors which have brought the men to a position of willingness to support a program of premedical care sponsored by a medical society. Going across the country, we know this action was precipitated in Michigan and in California by a very decided threat of passage of a law for compulsory health insurance.

Massachusetts sampled another type of pressure, although it wasn't serious, and it is similar to that which has appeared in Oklahoma City and in Washington, D. C., and that is the appearance of the consumer cooperative. The other motive—it was preexisting in Massachusetts before the appearance of the consumer cooperative movement—was a determination on the part of the profession to accept the fact that there was a problem in the distribution of the cost of decent medical care, and that they were accepting it as a responsibility and were going to try to find a solution for it.

In the achievement of support of the profession, I just briefly outlined how we accomplished what we have accomplished to date in Massachusetts. I think it is a fairly satisfactory start, because of the effect on practicing physicians. I think within six weeks we have achieved an enrolment of well over 50 per cent.

The approach was this: We had a special committee which was empowered to work out the program for starting the corporation. They had to report through the various committees, the council and our legislative body. The proceedings of the council were published in the *Journal*. That was read I think—I doubt how widely—by the practicing members of the state, because some are interested in proceedings, and many are not.

In the realization of that weakness and that approach, last year all the district societies were approached and spoken to along three lines: first, the need of such a plan from the point of the threat which faced us; second, a specific discussion of the type of corporation that was going to be created from the point of view of the interest of the physician as to whether or not he was going to lose control over the practice of medical care as far as basic medical problems are concerned; and, third, the financial problems which always interest the physician and are involved in the two fundamental questions of cost to the public and the fee schedule for compensation to the physician.

This was followed up, when all data were approved by the commissioner of insurance, by the circularization of every physician in the state with a brochure. Through the summer we got out these separate supplements, apart from the *Journal*, for fear any such information would be lost in the depths of the *Journal*. When everything was ready we circularized the physicians with a brochure, with information containing the basic philosophy in back of it, all data, by-laws, subscriber's contract and the rules and regulations, so that before we asked a single physician to participate in the corporation he at least had available every bit of information which, as an intelligent man, he was entitled to have before we asked him to sign a contract.

Simply mailing the data brought us 1,400 men. We followed it up in a few weeks with a postcard, knowing that the doctor's weakness is to place all mail under the pile of issues of the *Journal*, and we acquired another thousand signatures. We followed that a week later with a pressure letter, and we have over 50 per cent of the active men in the state at present. We are going to follow that with active solicitation within the next few weeks by the lay members of the Blue Cross, helped by committees of physicians who are appointed in every district in the state, and it is our hope that before we effectively start the sale of this contract we shall have enrolled 60 to 75 per cent of the physicians within the period of two months. That, of course, remains to be seen.

Next comes the basic problem of how you are going to establish this type of corporation. There have been many approaches in all the states through the country. One state will set up these corporations in small areas, even in cities; other states have set them up on a statewide basis, as have California, Michigan and Massachusetts. Others require that, before a statewide corporation can sell in a district, it has to have the approval of the local group. Massachusetts has not accepted that as a safe approach from the point of view of securing sales of an adequate number of contracts. This matter was threshed out recently in Michigan, after a year and a half of functioning, and the house of delegates there voted "No" on a censorship—which it amounts to—by the districts as to whether, after the state sociey has started the venture, it should be sold in their sections.

Another problem that must be looked at very carefully is whether or not this type of corporation is going to function in a rural area, an industrial state or a state that has a balanced economy as far as industry and agriculture are concerned.

We have an urban problem of 94 per cent, and a rural farm problem of 1.6 per cent. On the basis of wage earners, which this primarily involves, we have 35 per cent of the industrial manufacturers, our retail group 19 per cent, and all industrial activities represent but a small percentage. So, immediately our problem broke down on the fact that we had primarily an industrial problem and, secondly, a retail sales problem. Breaking it down into geographic areas, we found that our wage earnings were only 36 per cent in metropolitan Boston in the industrial group and 64 per cent in extrametropolitan Massachusetts. In other words, the whole state looms very large in this problem, as compared with the important metropolitan area.

As to the type of organization, since enrolment is related to the number of people whom you can procure in a single group, we found that 75 per cent of our wage earners were in industries employing from 100 to 1,000 and over. We don't get much over for an organization like General Electric, which now is employing 18,000 or 19,000 people, whereas in Michigan General Motors delivered a subscription list to their cause of 160,000. Again, these larger organizations are distributed between 75 and 80 per cent in extrametropolitan Boston.

You make very important commitments when you undertake a project like this, and I think one of the most important ones is that we go before the state legislature and ask for an enabling act. I think I can very quickly give you the import of what it means to have a law put on the books, when I quote this from the recent address of the president of the Pennsylvania State Medical Society:

> Even now, threats can be heard of legislative action to modify our own enabling act to place its control under the state. This must be anticipated by early action on our part.

So we cannot be afraid of proceeding on the basis of legislation. I don't think doctors would undertake the risk or assume the risk of forming such an organization, nor do I think you could have the cooperation of the stable type of citizens in putting across such an organization as this unless we had the basic protection afforded by the law of the state.

There are other important commitments to which you are going to give your hand in the simple process of getting an enabling act. First, you are going to determine the eligibility of physicians to participate in the program, and that is directly related to the problem of standards of medical care. That may not be a large problem in some states. It was a very difficult problem in the state of Massachusetts. The osteopaths in our state are licensed as physicians under the same law that we are licensed. There are only 270 of them, but in the state of Maine, where they have their own licensing law, they are flooding the state. Our enabling act is so worded that they will continue to participate. I don't believe we could have had a law from the legislature unless any licensed physician could participate.

We are also faced with the problem of substandard schools in Massachusetts. We have had two of them. It is a problem that other states do not face at all, but I heard Elliott Joslin, whom you all know, the authority on diabetes, stand on the platform and make the statement that if it were not for the graduates of the substandard schools the other schools could not supply the numbers of physicians needed in the state of Massachusetts, and there would certainly be inadequate medical care if we went short on the number of physicians. For years the profession has fought to have that situation corrected, but it is filled with many implications that can't be brushed aside by the statement that we won't qualify the men who are graduates of substandard schools. Also when the Army is not taking the substandard school but is taking the standard school graduates, the proportion of substandard school men has risen on a percentage basis in the state of Massachusetts.

Another problem you introduce when you ask for an enabling act is the question of supervision of your corporation, and that is serious. Is it going to be under public welfare? Is it going to be under public health? Is it going to be under insurance? Most state societies have chosen insurance because, I think, knowing physicians, we would hesitate to see in our name the accumulation of the vast public funds which will be accumulated unless it is watched by an organization like the State Department of Insurance. There is no question that its point of view is that of insurance and not of medicine, but the practical facts remain.

We have faced this problem of the insurance point of view being interjected. I think so far we have come along fairly satisfactorily. When you put it under the Department of Insurance and work through a state bureaucracy, you make another interesting observation. You can work for months and establish basic plans and premises and then find that in two minutes, when it is put on the desk of the Commissioner of Insurance, he doesn't accept the word and advice of a subordinate, and it is thrown out the window.

We had to sit and argue to keep the osteopaths from writing a clause into our own by-laws. We had to have a formal hearing before the Department of Insurance. We put up $25,000 to start the thing. Under the ruling of the department, at present we have $5,000 to start with. The rest is frozen. After we had our whole organization completed and ready to sell the public and the by-laws approved in May, we received a letter in September that they wanted to change the by-laws. I think we are going to stand our ground without any question.

Another important problem with regard to the enabling act is that you are going to determine very definite matters with regard to control of your corporation, so far as the medical profession maintaining its proper guidance on distinctly medical matters is concerned.

We have felt that, to have an effective board, it should not be too large. One of the men very honestly told me he thought at times that the meeting of his board looked like a medical convention. I think that will have influence on the support which the corporation is given by the public. We have this setup: one third of physicians, and this one third subscriber representation was a requirement of the enabling act. That is why this comes in. Then we have one third open, using here eminent laymen who can really give your corporation standing before the public and give the type of advice which is necessary in such a large effort if it succeeds.

How about the vital medical man? We have pulled out the one third physicians as a central professional service committee functioning within the board of directors. This seems to cover the things we are concerned about, and this group has the power, having advisory help from district committees, to initiate all actions on these matters into the board of directors.

I will say that working with these groups of laymen, and bringing our program to completion, as far as readiness to sell to the public is concerned, there has been no difficulty with reference to these matters which concern the profession. That assures a carefully studied and professional point of view as the basis for action on these matters, and so far we have been very successful and effective.

One question has been discussed very widely over the nation, and, of course, being an industrial state, it is a very important problem with us, and that is the representation of labor on the board of directors. Although organized labor may represent about 10 per cent of the working group of the population, nevertheless I heard an important member in a manufacturing organization state the fact that their organization did give them the power, because they accept the self discipline. Some of the states started without representation of labor, and they have told us they regretted it and are now moving into a position of representing labor.

I talked with the major manufacturing men, who were our representatives, and they were in agreement with the view that ultimately labor is going to have representation in all these organizations, and it is much better to pick the type of man you want in your organization in the beginning rather than to have him hand picked for you later and not have as satisfactory an individual.

There are other problems. There is the question of income limitations if we offer service contracts to the people. It is hard to see how a physician would become too enthusiastic

over working very hard to establish a pure corporation. I think people are looking for a setup where they will pay a premium and get a service, and Massachusetts Medical Service is based on the fact that fundamentally our medical service contract is the one we are interested in.

All over the country there has been a wide diversity of approach to this problem of group income limitation. It is an unsatisfactory problem at best. California has a level of $3,000 for eligibility. Buffalo has a level of $3,000. Utica has no level at all. New Jersey started with a level of $1,600 and found they had to raise it for practical requirements. You just couldn't enroll an adequate number of workmen to start such a corporation if that was the level. Michigan State established $2,500 for the family and $2,000 for the individual. Those same figures were set by the state of Massachusetts. The labor representative, when we had our first meeting, made the request that he thought it would be more equitable if the large family group was eligible up to the level of $3,000, because, in effect, the laboring group looks on $3,000 as the upper demarking line for the wage earner. Beyond that you get your foremen and men who have better positions in industry.

We found that in our manufacturing group the average income was $30 a week, in the retail group $22 a week. This was in 1941, before we had time and one half, and war industries came into the picture.

We found that the $2,000 limit for the individual took 83 per cent of the wage earners, and $2,500 for the family took 91 per cent of the wage earners of the state. To approach such a program with much lower levels would not really meet the problem. That is how we felt in Massachusetts. There is the question of whether, with the large family groups, it should be higher or not. It is an eminently unsatisfactory approach.

The employer in many instances has told us "We won't reveal the workman's income." They are going to now. Many of them have to reveal it through the income tax, and we considered whether or not the report through the income tax should be the level as a means for determining the income groups, and we were told flatly by the Department of Insurance that they wouldn't accept it. That is all there is to it. What the department tells you usually is the basis on which you function. The patient will state his level of income. We have to accept that at the time of enrolment, and if it changes the only method of determining that is when the patient comes in with his card, when the physician can ask "Are you still below or above this income situation?" That is an unsatisfactory situation, but there is none better until somebody finds it for us.

The next big question which disturbs many groups is Are we going in the insurance business? In other words, in addition to the service contract shall we have an indemnity type of contract above the level set for the service group? There are two reasons why I think we are forced to do it. The fluctuation of income in the state of Massachusetts through the years is now getting up into astronomical proportions. But if you take your median and put your large group enrolled right through here, what are you going to do to them in a year? They are back on the service, they are above it, they are back again. Are you going to enroll them next year and tell them "You are out" and then ask them to come in? This indemnity contract seems to be a buffer contract when they stay in the overage, but when they need service again it is available to them automatically.

The other point of view in the sale of these contracts is that you can't interest the group in industry unless you have something to interest the foreman, interest the man in charge of the group below, because the warmth you receive is in direct proportion to whether or not there is something in this proposition that interests the man at the top.

Now comes the major problem of the initial contract. What is going to be your type of approach? Massachusetts definitely accepted the approach that we would base our experience on the practical experience of the other states. As Mr. Simon said, they started out with the idea that they were going to give complete medical service right down the line. We learned from the groups that it couldn't be done, so we haven't attempted it. As a matter of fact, we were warned that the reasonable approach to this thing—they gave us figures—was through partial coverage and then endeavoring to develop it to complete coverage.

Massachusetts took the experience from all over this country, and I might say that the whole picture has changed with those who adopted complete medical coverage.

Michigan is selling a partial coverage contract. Buffalo or Utica, I am not sure which, is canceling complete medical coverage and selling partial coverage and, I believe, changing the indemnity basis. So we started in and said "We will take the type of coverage which is actuarially sound." I think you have got to do three things to start this thing. You have got a sort of tripod. You have your ideal, you have sound actuarial practice and you have what the public will accept and buy. Those bring you at present pretty much to a surgical and obstetric contract. When both types were offered in Michigan, 160,000 partial contracts of the surgical and obstetric type were sold as against 5,000 for complete medical care. That is somewhat related to the difference in premium costs. In our picture, starting with this surgical and obstetric coverage, it covers 62 per cent of the hospital care. When we are established on a sound basis we intend to extend it to a complete hospital coverage picture, which is the one which New Jersey is starting with at present, plus such coverage in the home and office as seems, from the experience of other groups and studies of our own, to be advisable.

That brings us now to the basic problem of finances. One problem relating to that is the question of correlation of this endeavor with the Associated Hospital Group, and that is a problem which is under development and, you might say, a matter which is under controversy in different sections of the country. That controversy is related to whether or not the Associated Hospital Group of the Blue Cross System and the Medical Plan Groups shall be intimately related or whether they shall be quite divorced. It is a very important problem.

One of the bases of criticism for compulsory health insurance is the cost of maintenance of the corporation by virtue of payments to lay members, and the statement about the large number of lay members involved in the German system of compulsory health insurance is one we know of and is quoted repeatedly. Are we going to place ourselves in the same position, of duplicating too much of cost in the way of duplicating personnel, duplicating office setup, in the distribution of our program? There are those who seem to identify the Associated Hospital insurance program with the Medical groups, in the fear that medicine may be taken over by the Hospital groups. In our section, at least, that is so. To me, I can only visualize the Associated or Blue Cross Systems as a financial intermediary between people and the hospitals, the same way that our corporation is going to be the financial intermediary between the people and the individual physician.

I just quote to show you how this problem is developing. It is a public statement, so I presume it is proper to quote a recent motion voted in Michigan: "That Michigan Medical Service be separated from Michigan Hospital Service at the earliest possible moment consistent with sound actuarial practice." It is a very difficult problem. Massachusetts is starting out with a very close and intimate tie between the two organizations. We have had the best of relationships there. I hope it will work out. Nobody can say it is right; nobody can say it is wrong. It is one of the questions that time has to show us the way. It seems to me that we are mutual allies. We are voting for the basic problem of preserving a voluntary approach to the problem of settling the costs of medical care on an insurance base, and I understand that in the recent hospital group it was the Blue Cross members who fought most forcibly to bring the hospital group to a definite stand on many problems relating to relationship with the government. I think we are protected by their position. If the voluntary scheme disappears, they go. If the voluntary scheme disappears, we shall probably be serving some other way, whether under the government or what not. So I think, maybe at the expense of giving the patients the greatest benefit for the premiums paid, if we separate too far from the group we may be jeopardizing our chances for success. That, of course, is entirely debatable, but it is the point of view on which we are proceeding.

The other important problem relating to finances is the question of the premium rate. Buffalo started with complete medical care, and considered the surgical. Utica, complete medical, and covering hospital and surgery. New Jersey started with complete medical care, and I think they are starting only with hospital and surgery. California, with a comprehensive plan, is restricting sales and is selling surgery. Michigan has canceled the comprehensive plan and is going to surgical.

I want to call your attention to the various premium structures: benefits allowed, fee schedule, the expenses, and the service that is created. That each of us should be stumbling along with no correlated body of knowledge with regard to these many difficult problems with which we are confronted, I think, is unfortunate. I just give you this to look at. The Blue Cross books are correlating in loose-leaf form the accumulating data of all their various plans. Yet Michigan, Massachusetts and California have a wealth of experience on a

definite social experiment in medical economics, but the knowledge isn't correlated so we can use it in the states. These many problems I have just outlined I thought you should know. Those of you who have been through it are well aware of them, but these basic problems we haven't yet organized so that we can get information on them. There is certainly no one answer to all of these problems, but the many difficulties the different states have gone through in tackling them, from the enabling act up to determination of premiums, I think might well be correlated, analyzed and put into printed form so that with the changing problem—you have seen how it has changed even in the states of California and Michigan, which have been in it for some time—we can strengthen each other by the experience of other states and not jeopardize this whole approach to the problem of prepaid medical care by repeating the mistakes of others and by wondering "Where can we get help on this specific problem?"

DISCUSSION

DR. WILFRID HAUGHEY, Battle Creek, Mich.: I know something about this Michigan plan. I have been on the committee that has been working for about four or five years developing it. I am vice president of the plan, because I refused to be president. I do not live in Detroit, where the office is. I live in Battle Creek, and it is a three hour trip to Detroit and three hours back again. In working this thing out, we had forty-four meetings in Detroit in one year, where we started in about 2 or 3 o'clock in the afternoon and finished about 2 or 3 o'clock in the morning. We had no data to go on. We had nothing to start with except our bare hands and what we had inside our noddles on insurance, which wasn't too much. It was a question of cut and try, as you have just been told.

This thing has been worked out in Michigan over a period of many years. Our Economics Committee made a very detailed survey of the state over a period of four or five years ended about 1930 or 1931 and brought in a report to the state society with a proposed plan. That was finally considered by the society in 1934 and rejected. Then our committee went to work again and we finally have a plan. We have had all the stumbling blocks you have just been told about, and some they haven't told you. We are still altruistic. We are still paying for all the surgery done in the hospital, and we are considering right now paying for some surgery in the office, because our hospitals are so full we can't get patients in. We haven't actually done it, but it has been authorized as soon as our administration thinks it can be done. You have been told that we have been ordered to divorce from Michigan Hospital Service. That is true. Our house of delegates voted to separate as soon as it is actuarially sound. I don't know when that is going to be, but what we are now considering is a third corporation to do the sales and to do the contact with industry, to make the collections and so on and then turn the money and the contracts over to Michigan Hospital Service and to Michigan Medical Service to work on.

We have over 455,000 people being taken care of. We had a revolt, as you were told. We had one county society that flatly refused to cooperate ever since we started, and they spread the gospel to about three others. There were three more counties on the fringe of joining that group, but at the last meeting of the state medical society in September we ironed out some of that—not all of it. We still have the unalterable opposition of certain groups. They will not fill out our blanks. They send their bills to the patient. The patient has to forward the bills to Michigan Medical Service and, up to about two or three weeks ago, they refused to accept our checks in payment. We had to send delegates to one of those counties to go with the patient to the doctor's office and pay in cash and accept receipts. We did that for a long time. We sent $15,000 or $20,000 up to the bank in that town under the Fidelity Insurance. The man couldn't carry more than $500 at one time, so he would have to go to the bank and get $500, pay that out, and go back and get some more. They sometimes had $15,000 and $18,000 to pay out during the trip up there, so you can see the nuisance it was. That county has finally voted to accept our checks, so we think we have that solved. They are not cooperating, but approximately 80 per cent of our doctors are cooperating.

We have changed the method of cooperation so that the doctor doesn't make any rash promises, and we are not holding him very closely to it. If he will participate and will render service and make reports, that is all we want. We are not too strict about that; that is, I mean his signing that cooperation list. We are paying a good big proportion of our funds out to noncooperating doctors in the idea that these people are covered by our plan and are entitled to the service and we should pay for it. If they go to a doctor who isn't cooperating, we pay for the service just the same. Two or three times, and once under the direct demand of the Insurance Department, we voted to not pay any more noncooperating doctors. We were getting along in pretty good shape at that time. We were beginning to see where we were getting pretty nearly up to black figures. Promptly we went back into the red, because everybody hustled in to get the work done before the date that they couldn't be paid for everybody, whether he cooperated or not. We have been through that two or three times. We put that off for sixty days and then went through it again. We have finally decided that we will not make any such statement any more; we are going to pay for the services. But we are up against another proposition. We asked for reports for these services within thirty days, and we are still getting some of them after two years. How can you make any actuarial plans when the doctor doesn't send in his bills for a year or two years? We have been told by the insurance commission that after a reasonable length of time we shouldn't pay those doctors. Where are you going to draw that line?

We started out with a rate that we charged for the services, and we have had to increase that rate. Last Wednesday night we voted another increase in that rate, which our actuarial advisers tell us will carry the load and ultimately get us out of the red. We are in the red; we admit it; everybody knows it. For about four or five months we prorated what we paid the doctors. We paid them 80 per cent of our allowances. We stopped that proration. We are going into the red. We are paying the bills as they come every month and yet actuarially and figuring reserves for bills that haven't come in yet, notices we have had from doctors that they have such and such a patient, it shows us in the red. We don't know whether we are carrying enough reserve for that or too much reserve for that. But our experience is that about 40 per cent of the notices we get that there is service being rendered to such and such a patient don't actually pan out into a liability that we have to pay. Maybe that patient didn't go to the hospital at all. Maybe there were a lot of things. Maybe the doctor simply made up his mind that he didn't need that money. We don't know why, but we do know we are notified of thousands of cases in the office that we never have to pay anything for, and those notices come in thirty days, sixty days, ninety days or a year late. We have set up a sort of plan, from our experience for two years and over, that we think estimates what the bills are going to be. We know which months of the year are the heavy ones and which months of the year are the light ones.

We think we have rendered a good service. We are paying our doctors fees that are commensurate with the fees they are getting in private practice. There are some items on which we may be low, and there are some items which we know are high, but we are trying to pay liberal fees for the service, and we are paying the same fees throughout the state, in industrial centers or in rural centers. We are doing that with the deliberate idea that some of the doctors in some of those districts weren't getting enough money, anyway.

I didn't tell you all about the start. There were two counties in our state that worked out a plan and wanted to put it into effect and were going to do it, when our state committee finally decided to go at it again. That information was all consolidated and worked out, and we actually started our work in Detroit.

Some of us wanted to put a restriction on elective surgery, not allowing elective surgery on preexisting conditions until the individual had been covered with his protection for a reasonable period of time. We didn't do it. We know now that was a mistake. We should have done it. Forty per cent of the money we have paid out to doctors has been for tonsillectomies and appendectomies, and we have paid out—I don't know the exact figure, but it is nearly three million dollars to our doctors since we have been operating. We are paying them about a quarter of a million dollars a month right now. That is big business.

We are way in the red. Some of you may know how much we are in the red. I am not going to tell you; I don't know. We had our whole affair audited by a group of nationally known auditors, which has just been finished. They couldn't audit beyond the first of July of this year, and in getting those figures they had to make tremendous numbers of estimates. They told us how much we were in the red then. The figures that were given us last Wednesday night showed, for the first time in several months, there was a balance in the black for the operation of that month. So we think we are beginning to see where we can work it out. A plan was given us, with some

little increases in premiums that we charge, and a considerable change in our operation, where we can pay off and get out of the red, we hope. The same actuaries told us eight or nine months ago that from the trend then we would be out of the red very soon, that we were getting out of the red at the rate of $20,000 a month at that time. Well, we were, but we weren't because, under orders from the insurance department, we told the nonparticipating doctors we weren't going to pay them any more, and promptly we went back in the red, way back in the red.

This is a problem that takes a tremendous amount of study, as you have just been told. We were wishing, all the time we were going through this thing, there was some bureau that had some information. There just wasn't any. This was a new thing entirely. We have information now; we have got plenty of it, California has plenty of it. I think we have more than they have. We are perfectly willing and anxious to sit in with any other states that are working on this thing and try to let them avoid the mistakes we made. We made mistakes, yes; we made plenty of mistakes. We did it honestly. We did it trying to do something for our people and trying to do something for our doctors. I think we are still making mistakes. I think we are covering too much ground in surgery. I still believe we shouldn't do all this elective surgery as soon as a family gets covered. We had one family that, within a month of taking out their policy, had seven tonsillectomies and three appendectomies and a hernia.

ALPHONSE M. SCHWITALLA, S.J., St. Louis: From the very beginning I have been critical of the whole Michigan Plan, and with a good deal of wisdom some of the people from Michigan asked me to come up and speak on the Michigan Plan at the first anniversary. I was very glad I could do so, because I acknowledged that I had been converted. But this last statement we just heard about being in the red perhaps might unconvert me, if this thing keeps on going, not that I think we should lose heart over the fact that there is a lot of red on some people's books, but, after all, this is an extremely difficult problem to solve. I don't have to tell you that. The very fact that these gentlemen who are running these plans are still clamoring for the experience of others, something to base their own experience on, is an indication of how difficult this problem is going to be to work out. In principle, I suppose it is possible to work out a scheme that is going to put medical economics on a sound basis and is going to harmonize the fundamental practice of medicine, the personal relationship between patient and physician and the responsibility of the individual for his own medical care and place that on a sound basis. Yet I am sure we have not as yet given enough thought in the nation as a whole to what we are about. That is the theoretical side. The practical side is an entirely different question. You know the menace that besets medicine today. There is no doubt about the governmental threat. You all know that the Social Security Administration has already in the back of its head forms for hospitalization care, medical care and compulsory health insurance that are going to apply to both sides of this question, the medical side and the hospital side.

I have a lot of feeling about this matter just now and, as I said, a week would not be too long to discuss this; but I think I would like to see the House of Delegates of the American Medical Association begin an evaluation of what has already been done, and I mean evaluation not only in the way in which they have done so already, by careful watching and careful study, but by some form of public pronouncement. I am not wise enough to say what they should say; I don't think any one of us is; but I think the combined wisdom of the Trustees and the House of Delegates just at this moment, that will give some direction to the state societies, would be an extremely valuable thing. I myself feel there is tremendous danger in state plans, and I say that on the basis of the experience of the hospitalization plans, the Blue Cross plans. I believe these plans should start locally, and as actuarial experience grows and as the homogeneity of a given area is going to be disturbed by the introduction of more foreign factors further afield, as modifications can be made in response to that experience, the plan can very well expand into a state plan. I say that because of the experience of the Blue Cross plans. Those have been most successful which have started locally and have expanded as actuarial experience could enable them to expand. In Dr. McCann's statements a few moments ago, about the big volume that the Blue Cross plans have gotten out, let's not forget that is the combined experience of about ten years, and that is the first time that kind of a volume has been gotten out, so don't get jealous of the Blue Cross plans. They do have this big volume out just now but, as a matter of fact, that volume has not been possible until just this moment.

I have a feeling that I wish we could put this whole scheme not into the insurance department of the state. I think the emphasis is wrong when it is put into the insurance department. I am sure of the fact that in some states—Michigan particularly, I think, had its difficulties with this question, and California had a notable difficulty—they could not get their plan under a welfare program. I would rather see it under a welfare program whenever possible. You will not be bothered under a welfare program, if the state laws permit it at all. In Missouri you would not be bothered with a $25,000 initial deposit. You would not be bothered by the actuarial restrictions, the accounting restrictions that are implied in an insurance scheme. You can run this on a very much less expensive basis if it can be put under one of the welfare departments of the state, perhaps even under the state department of health in some form or another through the creation —in many states, at least—of a subsidiary company of some kind. I have been afraid of the insurance patronage or control by the insurance department of the state for some of the reasons already indicated in Dr. McCann's presentation.

Many of the great drawbacks in costs have been because we have tried to give service in the costliest phases of medical care. One of the principles in hospitalization insurance has been to try to reduce the high costs of hospitalization by plans that are lower. They have left the hospitals to keep their own admission policies, and that has had the effect of equalizing the high cost in some hospitals by the lower cost in other hospitals. In some way or another I think the plans might have been more successful if the high costs of surgical and medical care had been diluted the wise way, by the lower cost of medical care given by the internist and by others who will not require the type of costly equipment that surgery requires.

MR. A. M. SIMONS, Chicago: The most encouraging thing today was Dr. McCann getting down to brass tacks and telling where you make mistakes. In great social experiments there is no other way to proceed.

DR. GEORGE H. KRESS, San Francisco: The Michigan State Medical Society and the California Medical Association have had similar experiences. We started out along somewhat different lines. They were much wiser than we in that they went in from the very beginning on a partial coverage plan. We went in on our idealist, full coverage proposition. We have practically completed our third year of operation. When we started, we asked the professional members, that is, the doctors —more than 5,000 of our 7,000 members went into the organization—each to pay $5. It was practically an admission or registration fee. That meant $25,000. The state medical association lent $50,000, which made a total of $75,000. Seventy-five thousand dollars is not a large amount of money to start anything that takes on the scope of an insurance agency, and yet, in one sense, that is what these medical service propositions are; they are expressions of the insurance principle. In California we worked out our procedure on the basis of unit values, and the basic unit we used was $2, the price of an office call. At the present time we are paying $1.50 on the unit, much to the unhappiness of a goodly number of our members, and, just as in Michigan, there have been insurrections throughout. Also in California we have had similar regrettable experiences because the men who insurrect are as loyal physicians as the rest of us, but they get off on these tangents. They feel that those operating the plans are not showing proper wisdom in methods of procedure.

The ceiling in California is $3,000. That has been a subject of great discord, because many doctors cannot understand why we should have so high a ceiling. But as has been said by one or more of the speakers today, unless you have a $3,000 ceiling and make it permissible to take in a number of $3,000 a year employees, you will not be able to secure the foremen and the higher priced shop men in these industrial groups who really set the sentiment for the other wage earners. Only recently the council of the California Medical Association has been forced to modify one of its rules, permitting the California Physicians' Service, under the auspices of the California Medical Association, in its own judgment to set aside the $3,000 ceiling as circumstances might indicate.

In the beginning, as stated before, we gave a full coverage. We are now liquidating our full coverage contracts and within six months there will be no further full compensation or full coverage contracts given by the California Physicians' Service.

We found through our three years of experience that by having what we call our deductible contracts, wherein the

patient pays for the first two visits, the amount of medical service was automatically cut down from 20 per cent to a 4 per cent basis. That is a very high percentage. With the partial surgical contracts and the partial medical contracts we believe real progress will be made.

In our hospitalization work we coordinate the efforts in conjunction with the three hospitalization groups that are existing in California. In the southern California agency the same administrative and sales distribution force takes charge of the work. We haven't been able to secure the same amount of harmony in the two northern groups, but in spite of all that progress has been made, and the California Physicians' Service is on a paying basis. It is true they still owe the California Medical Association $48,000, but that is a very small price to put up when you think or contemplate for a moment the great danger that was impending in that state in connection with compulsory health insurance.

I might call your attention also to the San Francisco Municipal Health Organization, with a coverage of some 16,000 municipal employees, where they also work on a unit basis and where they ran against the rocks. But by doing away with coverage for the dependents it has been possible to at last bring that unit up to par value. So these things can be worked out.

I must disagree somewhat with Father Schwitalla in believing that we must offer in the beginning a comprehensive contract, because in the very beginning—especially when members of the profession are the underwriters, the fellows who stand behind the gun to pay the bills, because that is what you do when you underwrite—it is absolutely necessary to put your proposition on an actuarially sound basis.

As you know, as you bring in thousands and thousands on the partial coverage plans and build up your reserves you can increase the amount of medical service you give. Of course, all of us must acknowledge that when we offer these prepayment plans and solicit in the beginning only those who are employees in groups of eight or more we have not yet reached the very lowest economic strata in income groups, and that is the problem ahead. But this is true: that these states that are doing this thing and carrying on this work—these constituent state associations—are amassing actuarial experience, and it is getting to be of a massive kind and getting to be very much worth while.

I am in full harmony with the proposal that it is time now for the American Medical Association to step in and see to it that the officials of these various medical service plans throughout the country are brought together, just as this group of editors and secretaries are brought together, so that it will be possible to amass the basic information that will prevent useless and unnecessary repetition of errors that some of us have made in the past. We have profited by the experience of Michigan, and we have profited tremendously by our own experience, and it is a foolish, ridiculous thing for any group of men, any group of physicians, any state association, component medical society or district group to embark on this kind of enterprise and do over again all of the foolish, idealistic things we are very prone to do when we take up the cudgels on behalf of an objective such as medical service for the lower income groups.

MR. LESTER H. PERRY, Harrisburg, Pa.: I might comment briefly on just one or two of the points brought out by Dr. McCann and make some suggestions for those of you who have not yet got really started. We are beginning our third year of operation and, like most of the other plans, we have found we have had to raise our initial premium rates. So my first suggestion would be that by careful actuarial studies set your rates as adequately as you can possibly determine in the very beginning. The second comment I have to make relates to the cooperation and coordination of the activities of a medical service plan with those of a hospital plan. We have members of our state society and members of the board of directors of the Pennsylvania Medical Service Association who are very skeptical of tying up with the hospital Blue Cross plan. They feel, as Dr. McCann mentioned, that perhaps the medical plan will be taken over by the hospital plan.

In studying this situation I did find out one fact which is rather significant. In the first place, I might say that in Pennsylvania we have a little more difficult problem in cooperating with the Blue Cross plan because we have five Blue Cross plans in the state, whereas in many of the other states there is one. Besides that, we have one rather large hospital plan which is not a Blue Cross plan. We have been cooperating with one of those plans to date and during the period of our operation their representatives, of course, sold the subscriptions to our service. During that period they themselves increased their membership by over 200,000. They got 10,000 subscribers for us. Of course the question is Why the big difference? One member of our board of directors feels that they sell the medical service plan only when they have to sell the medical service agreement in order to sell the hospital agreement. Whether that is true or not, I don't know. Nevertheless, the increase in their membership was twenty-three times the increase in ours. There are a number of other factors. One is the income limitation. The other is that in one of the large counties in that district we do not have the cooperation of the doctors and consequently have not attempted to sell in that county. In other counties we don't have what the hospital plan people think are enough participating physicians. My second suggestion would be that in cooperation with the hospital service plan, if you are sure you are getting real cooperation, go ahead, but at the risk of being a little cynical I would say be skeptical and look the thing over pretty carefully to see that you are getting real two sided, not one sided, cooperation. The third point I want to make relates to the question of supervision by an insurance department. In Pennsylvania we have a two prong supervision. Our enabling act gives the insurance commissioner the right to supervise our finances and our business affairs, but the secretary of health has supervision over all matters of a professional nature. That is the way we wanted it, and that is the way the act was written.

DR. NORMAN M. SCOTT, Trenton, N. J.: I hesitate to say anything on our brief experience, as we compare it to the experience in California or in Michigan. Nevertheless we did have the advantage of studying and observing the activities in California and in Michigan and Pennsylvania and Toronto before setting up our plan. Dr. McCann spoke of supervision by the insurance commissioner. To us that has been most valuable. We feel we can furnish all the medical knowledge that is necessary in these plans. Our great need has been for actuarial guidance. By proper approach to our commissioner of banking and insurance we had his complete sympathy on this effort. We sat down with him when we wrote our act, and he pointed out to us many points to be included in our act which would protect us under the laws of New Jersey. That, of course, was carried back to our legal advisers and to our own groups, but before this bill of ours went into the assembly the commissioner of banking and insurance was in complete accord and sympathy with us. He does not claim he has supervision over our plan. He doesn't like the word "supervision," but under the law he must see that we comply with the insurance laws of New Jersey. That is the only supervision he claims to have over our plan. If we should do something that was contrary to the law, he would let us know. So far he has notified us of nothing except that our contracts were according to the laws.

Dr. McCann spoke of participating physicians. I think you will find that in most states you have to recognize as participating physicians any who, under the laws of that state, are entitled to a full medical license. We cannot segregate one group of physicians from another. If they have the prerogatives of physicians, with full license to practice medicine, then you must accept claims from those physicians.

The question of income limitations was a great stumbling block in New Jersey. We at first established income limitations but have since removed all income limitations. That was done for a great many reasons. In the first place, you couldn't sell a plan in New Jersey, you couldn't interest industry in a plan in New Jersey which was discriminatory against any group within that industrial organization. If John Jones was an ambitious employee who took advantage of his overtime, promoted his own welfare, industry was interested in him as an individual, because by taking advantage of his overtime and opportunities he increased his income up to $2,500, $3,000 or $3,500 a year; whereas if, on the other side of the bench, there is a kind of good for nothing, the employer isn't particularly interested in him. He doesn't take advantage of his opportunities and is still making $100 a month. That is not the type of man industry is interested in. They are interested in the welfare of their best and most progressive employees. Therefore we have given up income limitations and have placed it on a bed occupancy basis. In other words, the money we pay to our participating physicians they accept as payment in full for services rendered, provided they admit their patients to a hospital for semiprivate accommodations. It is determined in the physician's office how he is to accept that patient,

and he signs the admission slip to the hospital under the hospital plan. If he signs an admission slip for semiprivate care, that is prima facie evidence that he understands he is to accept our fees as complete payment for the services rendered. On the other hand, if he believes this patient is of an economic status which entitles him to accept him for additional fees, he accepts him as a private patient, puts him in a private room and accepts as a credit against his bill the amount of our fee. That is done in an effort to put it in the hands of the physician.

Right now we have a tremendous group, especially of female employees, who are working for $20 and $25 a week who would be entitled to absolute full care under an income limitation. Still, their fathers, their mothers, their families are well-to-do people. As soon as those girls are sick, they put them in private rooms and get them day and night nurses. The doctor wouldn't understand why he is then required to accept our fee as full fee for the care of that patient. On income studies of the state we find that an income of $3,000, which is what industry felt we should place, would include 85 per cent of our population, whereas 35 per cent of our population accept private room care in our hospitals, thus placing a larger percentage of that group in the hands of the physician to determine whether or not he shall accept them as part pay or full pay patients.

I think some of these things should be defined. We are very loose in our terms. Complete service in Michigan and in California means—I think I am correct—home, office and hospital care. Complete service in New Jersey means that as far as our contract is concerned we give a complete service. Our contract is limited to medical service rendered while a patient is in the hospital, and while the patient is in the hospital we give complete service, medical and surgical. We do not think a satisfactory type of medical care can be rendered to a sick patient unless that patient has the advantage of medical consultation or unless a patient with pneumonia can be treated by an intern. Therefore we cover medical and surgical care if they are admitted to hospital, and we admit them to hospital for medical and surgical lesions.

There can be no question of the advantage of affiliation with the hospital plan. It would be a tremendous expense to set up as an independent organization a sales force, an accounting force or a claims staff. Those functions are parallel in our two organizations. Their salesmen are perfectly capable of selling our contract. They know the trade, as they say; they know where it can be sold. They are trained salesmen. Their accountants are trained accountants and their claim men are trained claim men. I think it is a tremendous advantage to have a very close affiliation with these hospital plans on things other than medical—on the business side, the promoting side. We are not promoters, we are not salesmen, we are not accountants, and we need the advantage of their actuarial experience. They know who the safe groups are. Of course, the education of the physician is one of our greatest needs. We have a county that has voted not to cooperate with us. I am sure it is because they do not understand our philosophy or what we are trying to do to protect the future welfare of the practice of medicine.

I think I speak for my board in New Jersey when I say we don't feel these plans are going to answer the problem of medical care distribution. If we took in 50 per cent of the people in New Jersey, that wouldn't answer it. Still, that is more people than would be interested in paying for this on a prepayment basis. But we can develop an agency—we have the legal authority to develop such an agency—and its administrative methods can be extended to take over any federal plan which comes into our state. It is for that reason that we administer the farm plan. I would like to see every state agency operate the farm plan because it sets a precedent. It tells the federal government "Here is an organization that has the legal authority and the ability to administer our plans to the satisfaction of the medical profession." This very precedent will be of tremendous value after the emergency is over if federal funds are made available for medical care, if we can bring it under our own control. I think we can. As you talk to the people in Washington, they are anxious to know how they can please the medical profession, how they can get the cooperation of the medical profession. They know that no plan they may promote will be successful without the sincere cooperation of the medical profession. If we can show them that we do have the ability, that we do have the legal authority within our state to handle federal funds—which is another thing that should go into our enabling act—the authority to accept and disburse federal, state, county or municipal tax funds in payment for medical care, that will be of tremendous value. That should go in every state act. We are lost if we don't have that authority on the state level. We have it in our act.

Briefly, what has our experience been since July? Our hospital plan went on sale in July. Our subscribers number about 5,000. We have limited our subscribers to cross sections of groups containing 100 or more employees. We haven't gone down into the smaller groups, except in two or three instances where they came in 100 per cent. We don't pay for tonsils for eleven months. We don't pay for obstetrics for eleven months. We set up reserves for them. For our first three months we paid 80 per cent and announced it in advance. The 1st of October we started paying 100 per cent, and we brought up to 100 per cent the partial payments we had made to physicians before. So we are in the black. We have a surplus of about 20 per cent of our earned subscription income. We haven't had enough experience, of course, to tell what we are going to be like six months from now or a year from now. We are negotiating with some larger groups, which is one reason we have not expanded more rapidly. We would rather take in two or three larger groups and set it at that for the year, perhaps 25,000 or 30,000, enough to support our agency, and study that group before expanding further. Most of our activities are limited to northern New Jersey.

There is one thing that came up here today, the dissemination of knowledge and experience. One of the greatest needs we have felt is proper accounting reports from the various plans. We get your bookkeeping statements, your financial statements, but as doctors we can't add 2 and 2 and make it come out 4 when it looks like 7 or 8 or 5. We can't make sense out of a bookkeeper's statement. We have this last month completed the form for a monthly accounting report which parallels, in substance, the annual report required by the commissioner of banking and insurance in all states, but brought down to a monthly basis so that it shows our actual reserves, our actual payments, actual cash on hand, which splits up our claims, our disbursements, our costs and so on. I wish every plan would work out something of that sort, and I would be glad to give you our form as it has been developed. I think it could be made a common form, because our reports to the commissioner of banking and insurance are common reports.

RADIO BROADCASTS DOCTORS AT WAR

Radio broadcasts Doctors at War by the American Medical Association in cooperation with the National Broadcasting Company and the medical departments of the United States Army and the United States Navy will begin on December 26 at 5 p. m. Eastern War Time (4 p. m. Central War Time, 3 p. m. Mountain War Time, 2 p. m. Pacific War Time). An exception is the Chicago area, where the broadcasts will be heard by transcription at 8 p. m. Central War Time Saturdays on station WMAQ.

Titles, subjects and guest speakers for the first four programs are as follows:

December 26. Give Your Blood to a Soldier, the story of battle casualties, evacuation of wounded and the use of plasma.
Guest speaker Major Gen. James C. Magee, Surgeon General, United States Army.

January 2. Nurses at Home and Abroad, the story of the army nurse and the nursing situation in home communities.
Guest speaker Capt. Ida M. Danielson, Army Nurse Corps, Director of Nurses, Sixth Service Command, United States Army.

January 9. Men Who Die in Vain, important factors in industrial health.
Guest speaker Dr. Stanley J. Seeger, chairman, American Medical Association Council on Industrial Health.

January 16. Stand By for Casualties, the doctor in the Navy.
Guest speaker Rear Admiral Ross T. McIntire, M. C., Surgeon General, United States Navy.

Titles and subjects will be announced in advance in THE JOURNAL. Names of local stations should be ascertained from local newspapers. The National Broadcasting Company, which formerly operated the Red and Blue networks, now has only one network, which is known as the National Broadcasting Company. The Blue Network is now independent of the National Broadcasting Company. Doctors at War can be heard only over the network of the National Broadcasting Company.

MEDICAL LEGISLATION

DISTRICT OF COLUMBIA

Bill Introduced.—H. R. 7856, introduced by Representative Randolph, West Virginia, a bill to provide for the registration of births in the District of Columbia that were not registered when the births occurred in the District.

Changes in Status.—H. R. 7522 has passed the House and Senate, a bill to amend the District of Columbia appropriation act, 1943, so as to authorize the use of public school buildings in the District of Columbia as and for day nurseries and nursery schools. H. R. 7781 has passed the House and Senate, a bill defining the real property exempt from taxation in the District of Columbia. Buildings belonging to and used in carrying on the purposes and activities of the Medical Society of the District of Columbia will be specifically exempted from taxation, as will be hospital buildings belonging to and operated by organizations organized not for profit.

MEDICAL BILLS IN CONGRESS

Bill Introduced.—H. R. 7836, introduced by Representative Izac, California, proposes to authorize the Secretary of the Navy to construct and the President of the United States to present to the people of Saint Lawrence, Newfoundland, on behalf of the people of the United States, a hospital or dispensary or other memorial as a token of appreciation of the action of the people of Saint Lawrence in saving the lives of officers and men of the United States ship *Pollux* and the United States ship *Truxton,* wrecked near Saint Lawrence in 1942.

Changes in Status.—S. J. Res. 140 has been reported to the House, granting permission to Hugh S. Cumming, Surgeon General (retired) of the United States Public Health Service, to accept certain decorations bestowed on him by the republics of Colombia, Haiti and Chile. S. 2769 has passed the Senate and House, a bill to authorize the rank of rear admiral in the Dental Corps of the United States Navy. H. R. 6730 has been reported to the Senate, a bill to prohibit interstate commerce in dentures in violation of state and territorial laws. This bill was passed over when reached on the Senate calendar, December 11. H. R. 7633 has passed the House and Senate, a bill to increase the pay and allowances of members of the Army Nurse Corps and to provide for the inclusion in the Medical Department of the Army of such female dietetic and physical therapy personnel as the Secretary of War may consider necessary.

MEDICAL ECONOMIC ABSTRACTS

MEDICAL AND DENTAL CARE BY STATE AGENCIES

The great expansion in recent years of medical care by state agencies is described by Joseph W. Mountin, Assistant Surgeon General, and Evelyn Flook, United States Public Health Service, in the August 21 issue of *Public Health Reports.* Medical care programs "include those offering treatment for either acute or chronic illnesses, irrespective of whether general or highly specialized medical or surgical care may be involved."

Eight departments of state governments are listed by name with the miscellaneous classifications of "others" as participating in such medical care programs. Every state and territory has one or more departments so engaged. The principal classifications of such care include general medical care of the needy, services for crippled children, cancer service, pneumonia service, and prevention and care of blindness.

General medical care is most frequently provided by departments of welfare and state university hospitals, "although hospital commissions, independent state general hospitals and health departments also function for this purpose in certain jurisdictions. As a rule, the medical care afforded is not organized as a distinct and separate entity but is merely allowed for as one item of a generalized public assistance program which also includes provision for food, shelter and clothing."

A wide variety of plans are in operation often within a single state:

"Physicians may be compensated according to a set fee schedule, they may be employed on a full or part time salary basis, or there may be in operation some sort of scheme whereby a central fund is built up from periodic contributions of those covered by the plan. Rates are sometimes determined by the state and sometimes by the local community. Usually the medical care contemplated is that which might be given by a general practitioner in his office, plus emergency surgery. Service is sometimes restricted to professional ministrations and sometimes extended to include drugs and supplies. Finally, economic eligibility for service is defined in such varying terms as 'clients of general relief,' 'medically indigent,' 'those unable to pay privately for needed care,' and 'wards of the state.' One state facility goes so far as to designate actual income limits, while other governmental units of the same state offer similar medical service under more general economic restrictions. Residence requirements also reflect the individuality of states and even of their subdivisions."

Owing to the "multiplicity of practices, it is difficult for a state agency to maintain supervisory control over local systems of general medical care." Thirty-six states participate in the provision of general hospital care on either a free or part pay basis for needy patients. Eight of these states supply the services through state operated hospitals exclusively. Some states provide hospital care wholly at state expense. In others, county and state share expenses. Iowa, Louisiana and the District of Columbia operate a fleet of ambulances for free transportation to and from the state hospital. The arrangements for special services such as for crippled children, cancer service, pneumonia and prevention and care of blindness vary widely from state to state.

Most state departments of health give some attention to dental health. Some complete dental health programs embrace both children and adults, but the attention of state health departments is usually confined to children's dentistry and education measures. The dental activities are being quite rapidly extended, seven new departments having entered this field of activity during the last two years. Most states give some sort of dental service in school systems. Some state health departments operate "healthmobiles" or dental trailers which constitute motorized dental clinics. In other states traveling health department dentists set up temporary clinics in a room of the school being served.

It is estimated that "two thirds of the $285,715,800 expended for composite state health services is charged to health programs which, primarily, are identified with maintenance of facilities for correction or care of mental and physical disabilities. Expressed otherwise, over 190½ million dollars are disbursed annually by agencies of state government for health activities in which medical or custodial care is the preponderant component. This figure, it will be recalled, is exclusive of medical benefits paid through workmen's compensation channels and of expenditures for tuberculosis and venereal disease, which also involve a considerable amount of medical care." The amount of expenditures varies directly according to the health of the states. The hospitalization for mental disorders alone accounts for nearly $145,000,000. Owing to the combination of various agencies it is difficult to give exact financial facts, and it is believed that the amount reported as being charged to medical care is extremely conservative. This includes the cooperation of state university hospitals, general laboratory services for pneumonia control, and certain measures in cancer control and the prevention of blindness.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

State Medical Board Election.—Dr. Percival Dolman, San Francisco, was recently elected president of the state board of medical examiners to succeed Dr. Fred R. DeLappe, Modesto. Dr. George Thomason, Los Angeles, was named vice president and Dr. Charles B. Pinkham, San Francisco, was reelected to serve his thirtieth year as secretary-treasurer of the board.

Baby Blood Bank.—The Irwin Memorial Blood Bank of the San Francisco County Medical Society has adopted a new service, a baby blood bank, consisting of half pint bottles of specially prepared baby-strength blood which are being made available to infants requiring transfusions in the San Francisco Bay region hospitals. The plan was started to conserve blood and to provide a higher quality service to infants. *California and Western Medicine* states that formerly, when the adult size full pint bottle of blood was furnished to babies, about half the blood was not required and was often wasted, and, furthermore, the anticoagulant concentration of sodium citrate used in adult transfusions was not always entirely satisfactory for babies. The new special half pint bottle with a lower anticoagulant concentration is found to be just right for infants, it was stated.

COLORADO

Society News.—The El Paso County Medical Society was addressed at the Camp Carson Base Hospital, November 13, by Lieut. Col. Philip S. Hench on "Management of Chronic Arthritis."——Dr. Lynn J. Lull, Denver, showed a motion picture on syphilis before the Fremont County Medical Society in Canon City, November 23. Dr. Vardry A. Hutton, Florence, who has retired from active practice, was elected an honorary member of the society at this meeting.

CONNECTICUT

New Million Dollar Hospital.—The dedication and formal opening of a new addition to the Hospital of St. Raphael, New Haven, took place October 24. According to the state medical journal, the structure, representing an expenditure of $2,000,000, is essentially a complete new hospital, for all patients will be cared for in the new building while the present structure will be left for service purposes. The new hospital is six stories high in the middle section with corresponding wings of four and five stories each on either end. On the first floor are the administrative, library and pediatric departments. On the upper floors are private rooms and wards of two to six beds, diet kitchens and utility and retiring rooms. The surgical division includes six operating rooms with the most recent type of air conditioning. The main kitchen, storerooms and utility rooms are housed in the basement, which also includes a coffee shop for the staff and visitors. In the main reception hall is hung a recent portrait of Dr. William F. Verdi, chief surgeon of the hospital, painted by Deane Keller, New Haven, and a gift of Mr. George Dudley Seymour, lawyer, New Haven.

DISTRICT OF COLUMBIA

Anniversary Meeting of District Society.—The Medical Society of the District of Columbia held a special program, December 9, to commemorate its one hundred and twenty-fifth anniversary. Dr. A. Magruder MacDonald, president of the society, gave the introductory remarks. Dr. Arthur C. Christie, past president of the society, spoke on "Medicine in the Nation's Capital, 1817-1942" and Dr. Frank H. Lahey, Boston, formerly president of the American Medical Association, "American Medicine's Contribution to the Nation."

Latin American Visits United States.—Dr. Miguel E. Bustamante, director of the Institute of Public Health and Tropical Diseases of Mexico City, arrived in Washington, November 11, at the invitation of the Department of State for a two months visit to scientific and research centers in this country. His trip will take him to the National Institute of Health, Bethesda, Md.; Vanderbilt University, Nashville, Tenn.; Department of Biology, University of Chicago; Rockefeller Institute Laboratories in New York; health organizations in rural Minnesota; Rocky Mountain Spotted Fever Laboratory at Hamilton, Mont., and the department of tropical medicine of Tulane University of Louisiana School of Medicine, New Orleans.

FLORIDA

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Florida is required by law to register annually on or before January 1, with the secretary of the state board of health, and at that time to pay a fee of $1. A licentiate failing to register annually is liable to a fine of not more than $50.

Dr. Griffitts in Charge of Health Unit.—Dr. Thomas H. D. Griffitts, who until his recent retirement was chief quarantine officer of Puerto Rico and the Virgin Islands with headquarters in San Juan, is now health director of the consolidated health unit in Dade County in Miami. Dr. Griffitts was connected with the U. S. Public Health Service for a number of years.

Activities of State Council for the Blind.—At a recent meeting in Tampa of the advisory committee for the Florida Council for the Blind, the members voted to give their services without remuneration for the duration of the war or until such time as a single consulting ophthalmologist can be employed by the council, and they agreed to invite other ophthalmologists to advise and assist the council on a volunteer basis. It was also agreed that the members of the state medical and dental associations be requested to provide general physical and dental examinations without charge, the council to assume responsibility for payment of the cost of material used. It further decided at this meeting to divide the state into three sections, the members to assume responsibility for expansion of the medical features of the sight conservation program in their respective districts. Plans were also formulated to obtain eye examinations and corrective medical or surgical treatment for the needy residents of the state.

ILLINOIS

Special Society Elections.—Dr. Joseph A. Fisher, Metropolis, was chosen president of the Southern Illinois Medical Association at its sixty-eighth annual meeting in Marion, November 5, and Dr. Willis I. Lewis, Herrin, was elected secretary-treasurer. Anna was selected as the place of meeting of 1943.——Wellington P. Shahan, Springfield, executive secretary of the Illinois Tuberculosis Association, was elected president of the Illinois Public Health Association during its recent annual meeting in East St. Louis. Clarence W. Klassen, B.S., Springfield, chief sanitary engineer of the state department of public health, was chosen vice president and Dr. Edward A. Piszczek, Chicago, health officer of the Cook County health unit, was made secretary-treasurer.

Chicago

Another Hotel Quarantined for Venereal Disease.—The city department of health quarantined the Harmonia Hotel, 3000 Indiana Avenue, December 10, on a charge of being a source of venereal infection among both civilians and men in the armed forces. Thirty regular residents of the hotel were enjoined from leaving the premises by the quarantine, newspapers reported. Sixty-one cases of venereal infection have been traced to the hotel in recent weeks, it was said.

Branch Meetings.—Dr. Milton G. Potter, Buffalo, discussed "Management of Breech Deliveries with Practical Demonstrations" before the Englewood Branch of the Chicago Medical Society on December 1. At a meeting of the North Side Branch, December 3, Capt. William E. Eaton, medical director, U. S. Navy, spoke on "Medical Service in the Destroyer Force" and Major Thomas Donald McCarthy, M. C., U. S. Army, "Hawaii Before, During and After the Attack on Pearl Harbor."

Meeting on Industrial Medicine and Surgery.—The Central States Society of Industrial Medicine and Surgery devoted its midwinter scientific session in Chicago, December 11, to war surgery and allied subjects. Among the speakers were:

Dr. William R. Cubbins, Compound Injuries.
Dr. Harold C. Voris, Head Injuries.
Dr. Italo F. Volini, Sulfon Drug Therapy.
Dr. James J. Callahan, Demonstration of Cases.
Dr. Raymond W. McNealy, Vascular Injuries in Reference to War.
Dr. George L. Apfelbach, Contaminated Wounds with Gas and Tetanus.
Dr. Milton H. Kronenberg, The Problem of Nutrition in Industry.
Harold A. Hooper, D.D.S., Mouth to Mouth Absenteeism.
Dr. Hedwig S. Kuhn, Hammond, Ind., Visual Testing in Industry.
Major William J. McConnell, War Department, Hygiene Supervision of Ordnance Plants.

The dinner session was addressed by Colonel Norman T. Kirk, M. C., U. S. Army, on "War Surgery."

Society News.—Dr. Wilber E. Post will deliver the presidential address before the Institute of Medicine of Chicago, January 22, at the Palmer House on "The Problems and Management of Bright's Disease from the Viewpoint of a Clinician Over a Period of Forty Years."——The Chicago Society of Internal Medicine will be addressed, December 21, at the Drake Hotel in a joint session with the clinical section of the Chicago Heart Association. The speakers will be Drs. Geza de Takats and Newell C. Gilbert on "Study of the Clotting Mechanism by the Response to Heparin"; Drs. Louis N. Katz, Allan M. Goldman, Richard Langendorf, Louis G. Kaplan and Samuel T. Killian, "The Diagnostic Value of the Electrocardiogram Based on an Analysis of 149 Autopsied Cases," and Dr. George E. Wakerlin, Clarence A. Johnson, Ph.D., Edwin L. Smith, Ph.D., Woodrow G. Moss, M.S., Dr. Milton L. Goldberg and James R. Weir, B.S., "Treatment of Experimental Renal Hypertension."

MINNESOTA

Physician Elected to Congress.—Dr. Walter H. Judd, Minneapolis, was recently elected representative from the Fifth Minnesota District to the Congress of the United States. Dr. Judd has been a missionary in China for many years and more recently has been stationed at Fenchow, Shansi. He graduated at the University of Nebraska College of Medicine, Omaha, in 1923. Dr. Judd was one of seven Americans who at a meeting of the American Bureau for Medical Aid to China on October 27 received a medal "of honored merit" for wartime services to China.

Four Counties Accredited for Tuberculosis Control.—Stevens County was recently accredited for human tuberculosis control, making the fourth county in the state to be so classified in the cooperative program of the state medical association and the state department of health to accredit counties showing a tuberculosis mortality rate not to exceed 100 per hundred thousand of population and an incidence of tuberculous infection among seniors in high school not to exceed 15 per cent. Lincoln County was accredited on Dec. 11, 1941, Olmsted County on May 22 and Murray County on August 28. The mortality rate must be based on a five year average and the student rate on tests of at least 80 per cent of the senior students of the county.

MISSOURI

Dr. Graham Receives St. Louis Award.—Dr. Evarts A. Graham, Bixby professor of surgery, Washington University School of Medicine, St. Louis, was presented with the St. Louis Award, November 5, during special ceremonies in the mayor's office. The award is given annually by an anonymous donor to the St. Louisan credited with the most outstanding contribution to the community during the year and includes a $1,000 check and a certificate. According to the St. Louis *Globe-Democrat,* the certificate cited Dr. Graham for his basic achievements in developing pulmonary and hepatic surgery, his productive leadership as a teacher of students and practitioners and for his influence on surgical theory and practice, and in particular for his "comprehensive focusing of present knowledge on the treatment of war injuries, thereby making this information easily available to all surgeons for the conservation and rehabilitation of the victim of the carnage of war." Dr. Graham was born in Chicago and graduated at Rush Medical College in 1907. He has been professor of surgery at Washington University since 1919.

NEW JERSEY

Acting Executive Officer Appointed.—Edith L. Madden, office manager of the Medical Society of New Jersey, Trenton, has been appointed by the trustees as acting executive officer until an executive officer is selected to succeed the late Dr. Le Roy A. Wilkes, Trenton.

State Society Occupies New Home.—The Medical Society of New Jersey has recently moved its offices into the former home of Mrs. Ferdinand W. Roebling, 222 West State Street, Trenton. The offices are located on the left side of the first floor and consist of a reception office in which the files, membership records and working equipment of the office manager, editorial secretary and secretary to the executive officer are kept. The adjoining room, formerly the library, is the board room and journal office. The former solarium at the rear of the board room is the executive officer's private office. The other side of the first floor is at present being renovated and will be occupied by a local ophthalmologist when finished. The second and third floors of the building consist of bachelor apartments. The exterior of the building is of white stucco.

NEW YORK

Students and Teachers Cooperate in Control Program for Influenza Vaccine.—Students and teachers at Cornell University, Ithaca, recently cooperated in a two week experiment under the direction of the Army Influenza Commission to test new vaccines. Drs. Norman H. Plummer and Herbert K. Ensworth, both of New York, directed the experiment.

Report of Commission on State Hospitals.—For the first time in fifty years since New York State assumed care of the insane, the rate of increase of patients in residence in civil state hospitals has decreased, according to a report of the Temporary Commission on State Hospital Problems, appointed by Governor Lehman. Certain recommendations which the commission made and which have already been carried out account for the decrease. When appointing the commission, Governor Lehman stated that the annual increase had averaged 2,392 a year for the last ten years. The commission reported a drop in this number to 726 between July 1, 1941 and July 1, 1942, adding that for the four month period between July 1 and Nov. 1, 1942 there was an actual decrease of 78 patients. The report stressed as chief factors in this decrease the increased and earlier use of parole, the boarding out of large numbers of carefully selected patients in family homes and progress in testing and using new methods of shock treatment. The commission's work to date was done from appropriations aggregating $110,000 for general expenses and for additional professional assistance in putting its recommendations into effect in the state hospitals. The report listed the following subjects as still in need of study: the system of records and reports in regard to patients, admissions, the bearing of syphilis control measures on the future population of state hospitals, research as to possible relationships of inadequate nutrition to mental illness, and vocational training, adjustment and employment of patients after parole or discharge.

The annual increase in the resident population of the state hospitals for the ten years July 1, 1930 to July 1, 1940, averaged 2,392 a year. The per capita cost of maintenance of patients in the state hospitals for the year ended June 30, 1941 (not including construction costs), was $386.45. Of the 3,710 reduction in resident population, 231 represented patients transferred to family care who were still being maintained by the mental hygiene department. This leaves 3,479 as the actual reduction in numbers of patients to be maintained by the state. The maintenance of 3,479 patients at $386.46 a year amounts to $1,344,494.34. The average cost of building new state hospitals (before it became impossible to build them at all) was about $4,000 per bed. To construct buildings for an additional 3,710 patients, the number of which exceeds the census of each of several existing state hospitals, at $4,000 per bed, would amount to $14,840,000. This cost is actually postponed, or avoided indefinitely, to the extent that the reduction of 3,710 patients in the state hospital census can be maintained. The annual budget of the state department of mental hygiene and the state institutions for the insane, mental defectives and epileptics is one of the largest of the state departments, approximating $34,487,000, and for the state hospitals alone about $28,000,000 a year.

New York City

Dr. Conboy Named Chief Examiner for Board of Education.—Dr. John E. Conboy has been appointed provisional chief medical examiner of the board of education until such time as a test is held to fill the vacancy created by the retirement in 1941 and death of Dr. Emil Altman, Sept. 11, 1942. The test will not be held until after the war.

Course on Industrial Medicine.—The New York Post-Graduate Medical School announces a course on industrial medicine, January 11-15, under the direction of Dr. Harry J. Johnson. The course will be conducted by physicians in industrial medical practice in cooperation with the faculty of the medical school. Additional information may be obtained by addressing the director of the New York Post-Graduate Medical School, 309 East 20th Street.

Josiah Lilly Honored.—The New York Branch of the American Pharmaceutical Association held a dinner at the Hotel Pennsylvania, December 9, in honor of Josiah K. Lilly, Ph.G., Indianapolis. The Remington Medal was presented to Mr. Lilly at the dinner (THE JOURNAL, November 7, p. 777). Mr. Lilly is the twenty-first recipient of the Remington Medal. He was a student of Prof. Joseph P. Remington and graduated at the Philadelphia College of Pharmacy in 1882. He is 81 years of age.

Central Agency Urged for Advising Mothers.—On December 5 Mayor La Guardia's committee on wartime care of children reported that an immediate major need was a central organization but decentrally operated service for advice

and information where mothers employed in industry or about to be so employed may get definite information on facilities available for the care of their children. It was further recommended to the mayor that the proposed service also provide agencies to mothers seeking advice as to whether they should go into wartime industry, on either a full time or part time basis. According to the New York *Times* the report suggested that at least six of these centers be set up as a beginning and informed the mayor that "a quick sampling study of blocks throughout the city" would be undertaken at once to get reliable information on the extent of the need for additional nursery school facilities required for the child care program suggested by the mayor when the committee was organized in his office in October (THE JOURNAL, November 14, p. 852). The committee will function in cooperation with all private, educational, social and civic agencies in the areas served. It was also stated that there is a possibility that some private funds might be available for the information center program on an experimental basis.

OHIO

Changes in Health Officers.—Dr. Kenneth E. Bennett, Strasburg, has resigned as health officer of Tuscarawas County to enter the U. S. Army Air Corps. Dr. Burt A. Marquand, Dennison, will continue as health officer of Atchison until Jan. 1, 1944.——Dr. Robert A. Evans, Columbus, has recently been appointed health officer of Franklin County.——Dr. Harold F. Minshull, New Lexington, coroner of Perry County, has been chosen health officer of the county, succeeding the late Dr. Frank J. Crosbie, New Lexington.

Dr. Hoerr Named Visiting Professor at University of Southern California.—Dr. Normand L. Hoerr, Henry Willson Payne professor of anatomy and director of the department at Western Reserve University School of Medicine, Cleveland, has been appointed visiting professor of neuroanatomy at the University of Southern California School of Medicine, Los Angeles. According to *Science* he will be in residence in Los Angeles until February 1. While there he will conduct a course in human neurology and give several special lectures in southern California.

Academy States Position on Medical Service Plan.—In a recent statement to the press, the Academy of Medicine of Cleveland announced that the Cleveland Medical Service Association plan does not have the sanction or approval of the academy and further that the plan is a privately operated enterprise, with legal rights but no academy supervision. At a regular meeting of the board of directors of the academy, November 10, a special committee was appointed to draft a statement explaining the academy's relation to the medical service association. The release to the press was prefaced with a statement that medical insurance plans were voted down by the membership of the academy after four years of intensive study. The Cleveland Medical Service Association plan was incorporated when some members of the academy assumed leadership in drawing up such a plan for citizens of Cuyahoga County (THE JOURNAL, July 25, p. 1034) after a recent vote of the academy had rejected the approval of such a plan. Later an organization was set up in Cleveland to develop opposition to medical service insurance plans in the community which bears the name Association for Preservation of the Present American System of Medical Practice (*ibid.*, August 29, page 1516). On November 17, at a special meeting of the board, the special committee which drafted the statement on medical service plans was reorganized to include three members nominated by the Association for the Preservation of the Present American System of Medical Practice, three members to be nominated by the Cleveland Medical Service Association and a chairman to be selected by these six members, all of whom are to be voting members of the Academy of Medicine of Cleveland.

SOUTH CAROLINA

University News.—The Medical College of the State of South Carolina, Charleston, has announced that Andrew J. Geer, a drug wholesaler of Charleston, had established a $1,000 scholarship in pharmacy at the college to be awarded to some student who otherwise would be unable to pursue the course.

TENNESSEE

Personal.—Howard D. Schmidt, B.E., director of the division of sanitary engineering of the state department of public health, Nashville, has resigned to accept a position as principal sanitary engineer at the Institute of Inter-American Affairs for work in South America, newspapers reported November 26. Mr. Schmidt received his degree in engineering at Ohio State University, Columbus, Ohio.

Dr. Sachs Delivers Haggard Lecture.—Dr. Ernest Sachs, professor of clinical neurological surgery at Washington University School of Medicine, St. Louis, delivered the William D. Haggard Memorial Lecture at Vanderbilt University School of Medicine, Nashville, November 27. His subject was "The Essential Qualities of a Great Surgeon." The Haggard lecture was established last year by the Vanderbilt chapter of Alpha Kappa Kappa in memory of Dr. Haggard, who was an alumnus of the fraternity and professor of surgery and clinical surgery on the Vanderbilt faculty at the time of his death.

UTAH

New Professor of Obstetrics.—Dr. Adelbert L. Dippel, associate professor of obstetrics and gynecology at the University of Minnesota Medical School, Minneapolis, has been named professor and head of the department of obstetrics and gynecology at the University of Utah School of Medicine, Salt Lake City. Dr. Dippel graduated at the University of Texas Medical Branch, Galveston, in 1928; for a time he served on the staff of Johns Hopkins University School of Medicine, Baltimore, and has been a member of the faculty at Minnesota since 1940.

GENERAL

Association for Advancement of Science Postpones Meeting.—The meeting of the American Association for the Advancement of Science and forty-four of its affiliated and associated societies that was scheduled to be held in New York beginning December 28 has been postponed, in compliance with a direct request of the Office of Defense Transportation.

The President's Birthday Again Approved for Collection of Poliomyelitis Funds.—President Roosevelt has again approved the public celebration of his birthday in January for the purpose of collecting funds for the National Foundation for Infantile Paralysis. In a letter to Mr. Basil O'Connor, New York, president of the foundation, President Roosevelt stated that he felt that any "interruption in this work would be extremely inadvisable unless absolutely necessary."

Social Hygiene Day.—The annual observance of social hygiene day has been announced for February 3, according to an announcement from the American Social Hygiene Association, New York. A pamphlet entitled "Social Hygiene Takes Battle Stations" contains suggestions for community programs and gives an outline of the national social hygiene movement. The American Social Hygiene Association and its one hundred forty-five affiliated social hygiene societies and committees cooperate with other national, state and local voluntary organizations in the aim to curb and reduce venereal diseases. The new brochure states that during the first world war there were 157,146 more new cases of syphilis and gonorrhea among United States soldiers, sailors and marines than there were wounds in battle itself. Total absences from duty due to this cause kept the equivalent of 20,600 men out of the fighting for a whole year.

Dr. Lyght Named Director of Health Education of Tuberculosis Association.—Dr. Charles E. Lyght, since 1936 professor of health and physical education for men and director of the college health service, Carleton College, Northfield, Minn., has been appointed director of health education of the National Tuberculosis Association. He succeeds Dr. Harry E. Kleinschmidt, New York, who resigned last summer. Dr. Lyght has served for the last five years as chairman of the Tuberculosis Committee of the American Student Health Association. He is widely known as a lecturer on public health subjects and has contributed to many medical, educational and lay journals in the fields of tuberculosis control, student health and clinical medicine. In 1926 he graduated at Queen's University Faculty of Medicine, Kingston, Canada. In 1927 he joined the faculty of the medical school of the University of Wisconsin, Madison, as assistant professor of medicine. Dr. Lyght was also connected with the department of student health of the university, becoming chief physician in 1932 and director in 1936.

Winners of Mead Johnson Awards.—Drs. Howard A. Howe and David Bodian, who have been pursuing studies in poliomyelitis for several years, were presented with a prize of $500 during the annual meeting of the American Academy of Pediatrics in Chicago in November. A prize of $300 went to Dr. Harold E. and Helen C. Harrison, Ph.D., New Haven, for their "painstaking work on the excretion and absorption of phosphate by the kidneys." The prizes are known as the E. Mead Johnson Awards for Research in Pediatrics and are presented through the American Academy of Pediatrics. The prizes just awarded were for the year 1941. Drs. Howe and Bodian will continue their studies on poliomyelitis at Johns Hopkins University School of Medicine, Baltimore, where, under a recent grant from the National Foundation for Infantile Paralysis, a Center for the Study of Infantile Paralysis

and Related Viruses is being set up under the direction of Dr. Kenneth F. Maxcy (THE JOURNAL, August 1, page 1121). Both Dr. Harrison and his wife are on the faculty of Yale University School of Medicine.

Changes in Industrial Hygiene Foundation.—The Industrial Hygiene Foundation, New York, elected the following members to its board of trustees at the seventh annual meeting in Pittsburgh, November 10-11: Ned H. Dearborn, Ph.D., executive vice president and managing director, National Safety Council, Chicago; Philip Drinker, Chem.E., professor of industrial hygiene, Harvard School of Public Health, Boston; Lieutenant Colonel Anthony J. Lanza, M. C., U. S. Army, chief, Occupational and Military Hygiene Subdivision, Preventive Medicine Division in the Division of Industrial Health, Office of the Surgeon General; Dr. Clarence D. Selby, Detroit, medical consultant, General Motors Corporation. Other board members were reelected. The foundation also announced the recent appointment of John F. McMahon, executive secretary, as managing director of the foundation to succeed Harry B. Meller, Sc.D., Pittsburgh, who retired from active management because of ill health. Dr. Meller continues as consultant. Dr. Raymond Hussey of the Maryland State Industrial Accident Commission, Baltimore, was named to the medical committee of the foundation.

New Gorgas Medal Awarded to Military Physicians.—Three military physicians were presented with the first awards of the newly established Gorgas Medal at the Cosmos Club, Washington, D. C., December 15, according to an announcement by the Association of Military Surgeons of the United States. They are Brig. Gen. Jefferson Randolph Kean, M. C., U. S. Army, Washington, D. C.; Brig. Gen. Frederick F. Russell, M. C., U. S. Army, Boston, and Rear Admiral Edward R. Stitt, M. C., U. S. Navy, Washington, D. C., all retired. The awards were established recently by John Wyeth and Brother, Inc., Philadelphia, in memory of Surg. Gen. William Gorgas, whose work in preventive medicine made possible construction of the Panama Canal. The awards include large silver medals inscribed with a likeness of General Gorgas and individual checks for $500. The medal will not be an annual award but will be presented only when such recognition is voted by the association. According to the announcement, General Kean was cited for his aid in conquering yellow fever by initiating warfare in Cuba against mosquitoes in 1900, General Russell for first immunizing the entire army and reducing the typhoid peril to a minor problem, and Admiral Stitt for extensive research and writing on tropical maladies and their prevention. The medals were presented at special ceremonies at which Mrs. Aileen Wrightson, daughter of General Gorgas, was guest of honor and received a courtesy medal. The presentation followed introductory remarks by Frank F. Law, head of John Wyeth and Brother.

Fellowships in the Medical Sciences.—Fellowships in the medical sciences, similar to those which have been administered by the Medical Fellowship Board of the National Research Council since 1922, will again be available for the year beginning July 1. These fellowships, supported by grants from the Rockefeller Foundation to the National Research Council, are designed to provide opportunities for training and experience in research in all branches of medical science. They are open to citizens of the United States or Canada who possess an M.D. or a Ph.D. degree, and are intended for recent graduates who are not yet professionally established. In addition to these fellowships the Medical Fellowship Board administers two groups of research fellowships, made available through a grant from the National Foundation for Infantile Paralysis, Inc. The first group, open to applicants who hold either the Ph.D. or the M.D. degree, is for the purpose of providing opportunities for special training and experience in the study of filtrable viruses. The second group, open only to graduates in medicine who have completed one or more years of hospital experience in clinical surgery and are planning a career in orthopedic surgery, is designed to provide opportunities for training and research in those basic medical sciences which will be of particular value in furthering progress in the field of orthopedic surgery. Fellows will be appointed at a meeting of the Medical Fellowship Board late in February. Applications to receive consideration at this meeting must be filed on or before January 1. Appointments may begin on any date determined by the board. For further particulars concerning these fellowships, address the secretary of the Medical Fellowship Board, National Research Council, 2101 Constitution Avenue, Washington, D. C.

Plan to Improve Teaching of Tropical Medicine in Medical Schools.—The John and Mary R. Markle Foundation has given $25,000 to the Association of American Medical Colleges to finance a program for the improvement of teaching tropical medicine in the medical schools in the United States and Canada. Under the plan, each medical school will be offered an opportunity for two members of its teaching staff to attend a two month course in tropical medicine beginning January 4. The development of the program will be in charge of a committee on tropical medicine of the association consisting of Drs. Henry E. Meleney, Herman M. Biggs professor of preventive medicine, New York University College of Medicine, New York, chairman; Malcolm H. Soule, Sc.D., professor of bacteriology and head of the department, University of Michigan, Ann Arbor, and Dr. Hiram W. Kostmayer, acting dean, Tulane University of Louisiana School of Medicine, New Orleans. The Surgeon General of the Army has given permission for one representative from each school to attend the course in tropical medicine being given to medical officers at the Army Medical School, Washington, D. C. The course consists of a broad survey of tropical medicine and is intended for clinical instructors in medical schools. The department of tropical medicine at Tulane has agreed to give a special course in tropical medicine in which particular emphasis will be placed on the laboratory diagnosis, pathology, clinical aspects and prevention of tropical diseases. This study is intended particularly for physicians who will teach the laboratory aspects of tropical diseases. Each of these courses can accommodate thirty instructors from medical schools. Travel and living expenses and, in the case of the Tulane course, a tuition fee, will be paid from the appropriation of the Markle Foundation. The deans of medical schools have been asked to nominate instructors to attend these courses, and the response indicates that each course will have a maximum attendance. Preference will be given to the schools whose instructors are now least well prepared to teach tropical medicine.

It is recognized that there is also great need for instructors in medical schools to obtain practical experience in tropical medicine. Preliminary inquiry indicates that such experience can probably be provided in the American tropics later during the coming year. Candidates for such practical experience would be selected from among those who have completed the course at the Army Medical School or Tulane and other instructors who have had academic training but not field experience in tropical medicine.

The committee in charge of the project has also interested itself in the collection of teaching specimens and material for the teaching of parasitic and other tropical diseases in medical schools. The Army Medical School, with the cooperation of the National Institute of Health, Bethesda, Md., and other institutions, is developing a distributing center for such material. Information concerning the center is being sent to the medical schools with instructions for the procurement of material either locally or from the center. It is expected that, in addition to laboratory specimens of animal parasites, there may be available certain charts, lantern slides and motion pictures. The Office of the Surgeon General of the Army has offered to make available to medical schools information which has been collected on the distribution of tropical diseases throughout the world. Plans for editing this material are in progress, and it is expected that maps will also be prepared and made available to medical schools, showing the world distribution of the important tropical diseases. The Markle Foundation has made an appropriation of $3,000 to the National Research Council for the preparation of this material.

CANADA

New Professor of Obstetrics and Gynecology.—Dr. John Ross Vant has been appointed professor of obstetrics and gynecology at the University of Alberta Faculty of Medicine, Edmonton, succeeding the late Dr. Leighton C. Conn. Dr. Jermym O. Baker is associate professor. All are of Edmonton.

Course on Chemical Warfare.—McGill University Faculty of Medicine, Montreal, sponsored a course of lectures and demonstrations on chemical warfare, October 19-30, under the auspices of the director of civil air raid precautions. Dr. Israel M. Rabinowitch, associate professor of medicine at McGill and scientific adviser on chemical warfare to the federal office of civil air raid precautions, conducted the course.

LATIN AMERICA

Blood Plasma Bank in Cuba.—The American-Cuban Fund of Helping the Allies has donated a fund of $12,500 to the Medical Federation of Cuba to establish a blood bank in Cuba. Drs. Gonzalez de Mendoza Arostegui, Havana, and Moisés Chediak, Havana, were appointed by the national committee of the federation to study the organization and functions of blood banks in the United States preliminary to the establishment of the Cuban bank.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 14, 1942.

Traumatic Duodenal Ulcer

Sir Arthur Hurst, Mr. W. H. Ogilvie and Dr. C. Keith Simpson have reported in *Guy's Hospital Reports* an example of the rare production of duodenal ulcer directly by trauma. A man aged 39 who was admitted in October 1931 had had good digestion until June 1915, when he was kicked in the epigastrium by a horse. He sustained a big bruise and was unconscious for a few minutes. Some hours later severe abdominal pain and vomiting developed. Continuous pain and vomiting after every meal prevented work. In July his appendix was removed, but on leaving the hospital he had severe pain after every meal. In October 1915 gastrojejunostomy was performed. The pylorus was found constricted by a healed ulcer. After the operation he kept fairly well for a time and returned to his work as a metallurgist. But he was always liable to attacks of pain and diarrhea. He improved, but the trouble returned each winter from 1919 to 1922 and between times he had shorter periods of ill health. In 1923 hematemesis proved nearly fatal. He improved again until May 1925, when he had another severe hemorrhage. Partial gastrectomy was performed. No ulcer was found, but there was a healed scar at the pylorus, which was constricted. His health improved, but in the subsequent years he had at intervals serious hemorrhages in the form of melena. In July 1931 he had his tenth serious hemorrhage.

On admission he complained of epigastric pain after meals, but this could be prevented by leading a quiet life. X-ray examinations showed that the remaining portion of the stomach emptied rapidly but that some backflow took place as far as the duodenal bulb. A Pola-Moynihan gastrectomy was performed after adhesions had been divided. He made an excellent recovery. Ten years later, in 1941, he was in good health and had gone to America in a technical job for the government.

This is the only case of gastric or duodenal ulcer seen by the writers in which symptoms developed immediately after a local injury. Chalier and Desjacques (*Ann. de méd.* **14**:78 [July] 1923) described a case of hematemesis immediately after the kick of a horse in the epigastrium. M. J. Stewart (Hurst and Stewart: Gastric and Duodenal Ulcer, New York, Oxford University Press, 1929) found focal hemorrhages and laceration of the stomach in deaths from trauma, which might well have been the starting point of ulcer had the patient survived. Stewart also reported that a man who was crushed in the epigastrium by the fall of a mine roof complained of pain after taking food and perforation occurred three months later. At operation there was already intense peritonitis and he died two days later. The necropsy showed an early chronic ulcer on the anterior gastric wall.

The Destruction of Instruments in the Museum of the Royal College of Surgeons

The recent publication of "The History and Evolution of Surgical Instruments," by C. J. S. Thompson, honorary curator of the historical collection of the Museum of the Royal College of Surgeons of England, shows the damage done by German vandalism to the greatest collection of surgical instruments, new and old, in the world. These numbered about three thousand when disaster overtook them. In one air raid a few were injured by water and the council of the British Institute of Surgical Technicians undertook their repair, but before this was completed nearly the whole of the surgical instrument museum was destroyed in another raid. From the débris some two thousand were salvaged, of which about fifteen hundred and a small collection of Chinese instruments were in fair condition. The remainder, comprising most of the obstetric instruments, were badly damaged. As shown by his "Guide to the Surgical Instruments" in the Museum, Dr. Thompson has long been, in the words of the late conservator of the museum, Sir Arthur Keith, "recognized at home and abroad as an authority on all that pertains to the technic used by medical men of past times in the treatment of disease." He has traced in the collection the evolution of the scalpel from the Babylonians of 1000 B. C. through the Greeks and Romans down to modern times and similarly the evolution of the amputating knife, the saw and other instruments. The rescued instruments have, after temporary refurbishing, been stored in metal cases supplied by the institute, under the direction of which they will be renovated after the war by skilled craftsmen. Much of the damage of course is irreparable. Here is one phase of a war which is being waged not merely against peoples but against civilization itself by a nation which never tires of bragging about its "kultur." It is fortunate that Dr. Thompson's profusely illustrated books to some extent compensate for the loss of instruments in this great historical series.

Factory Accidents and the War

The entrance into war industries of a large part of the population has had a profound effect on factory accidents. In his annual report Sir Wilfrid Garrett, chief inspector of factories, estimates that accidents in factories cause a loss of over 50 million man hours each month and factory figures do not include mining, road and rail transport, agriculture and shipping. The health of factory workers has been well maintained, which is attributed largely to provision of meals in canteens. Women have taken up war work in immense numbers. There is no indication that their health has been adversely affected. But the unwisdom of employing women who have had children on work that requires undue strain on the abdominal muscles is pointed out. As might be expected, the war has been attended with a great increase in preventable accidents. The figures for the past four years are given in the accompanying table. The increase in factory accidents to women has been much greater than in the case of men. The number of all factory accidents to adult men was 134,752 in 1938 and 191,343 in 1941, an increase of 42 per cent. The number for adult women was 14,626 in 1938 and 42,587 in 1941, an increase of 192 per cent. But the liability to accident per capita was less in women than in men. The liability for men was 1 in 25 in 1938 and 1 in 20 in 1941; the liability for women was 1 in 105 in 1938 and 1 in 56 in 1941. The great increase in the liability of women can be explained by the large number who were new to factory work.

Preventable Accidents During Four Years

	Fatal		Nonfatal	
	Number	Increase % on Previous Year	Number	Increase % on Previous Year
1938.....	844	..	179,159	..
1939.....	1,104	17	192,371	7
1940.....	1,372	24	230,607	20
1941.....	1,646	20	269,652	17

Lord Nuffield Honored

Lord Nuffield's munificent gifts to surgery have often been reported previously. In appreciation the Royal College of Surgeons has conferred on him its honorary medal, a distinction given to only eighteen other persons in the last hundred and forty years. In making the presentation the president, Sir Alfred Webb-Johnson, said that, while it was true that great riches had no real use except for distribution, it was equally true that virtue and liberality in the present possessor were the most just and indisputable titles of nobility. Lord Nuffield

replied that nothing he had ever received had given him greater pleasure. What he had done for medicine and surgery was only what he considered he should have done. Mr. Ernest Brown, minister of health, said that too often givers who lavished money on expensive buildings showed too little concern for the men and women who were to use them. Lord Nuffield never made that mistake. Of all his gifts they would like to praise him most for two things: (1) establishing six professorships and two readerships at Oxford; (2) founding the Institute of Social Medicine.

BUENOS AIRES

(From Our Regular Correspondent)

Oct. 30, 1942.

Tuberculosis in Argentina

The Comisión Nacional de Tuberculosis was recently appointed by the government of Argentina as a branch of the National Department of Hygiene. The members of the board of directors are Drs. A. A. Raimondi, president, R. F. Vaccarezza, vice president, and R. A. Vaccarezza, secretary.

Dr. J. A. Triaca of the Sanitary Branch of the General Department of prisons and penal institutions studied the incidence of tuberculosis among prisoners and delinquents. Among 1,893 prisoners there were 29 with tuberculosis (1.53 per cent) and 150 with diseases of the respiratory tract (7.92 per cent). Among 1,509 delinquents there were 10 with tuberculosis (0.66 per cent) and 127 with diseases of the respiratory tract (8.41 per cent). In the whole group of 3,402 prisoners, tuberculosis was found in 39 (1.41 per cent) and nontuberculous diseases of the respiratory tract in 227.

Drs. A. A. Raimondi, J. Gallo and L. M. Bonfante of Buenos Aires took roentgenograms of the chest of 25,000 school children and discovered tuberculosis in 2,784 children. The disease was in evolution in 1.21 per cent of the cases and inactive in 10.1 per cent.

Drs. Gumersindo Sayago and Isaías Naput of Cordoba recently observed children who had been given BCG vaccine in the Instituto de Tisiología of that city. A group of 350 newborn infants had the vaccine from March 1937 to March 1938. It was administered by mouth. It was given during the first week after birth. It was administered during fasting and dissolved in tea or milk in a dose of 0.01 mg. every other day to a total number of three vaccinations. Another group of 50 newborn infants had intradermal injections of 0.1 mg. of BCG vaccine in 0.2 cc. of a vehicle. The highest figures of allergy among infants who had the vaccine by mouth were observed from the third to the fourth months. The highest allergy figures in the second group appeared between the first and second months after the injection. The minimal figures of allergy in infants in this last group were in the fourth and fifth months. The rate of mortality in vaccinated infants was 8.3 per cent in comparison with that of 15.6 per cent in nonvaccinated infants. The highest rate of mortality in vaccinated infants occurred during the first three months of life, whereas in nonvaccinated infants it was shortly after the infants reached the age of 1 year.

The prevention of tuberculosis in Argentina has made great progress. At present all the applicants to and employees in positions in which they are in frequent contact with the public are systematically observed for tuberculosis. All government employees report for periodic examinations. All applicants for government positions have clinical examinations, roentgenograms and tuberculin tests. The allergic workers are classified. Among 10,863 applicants for work who were examined for tuberculosis, a positive diagnosis was made in 104. Fifty-one individuals were accepted to work with temporary certificates while they were under antituberculosis therapy. The group of 10,708 healthy applicants was observed for two years and tuberculosis developed in 6. Before a system of examinations was adopted for workers, the average frequency was 520 per hundred thousand individuals, which is ten times as much as that observed at the present time.

TYPHOID IN CHILE

Dr. H. San Martin Ferrari recently studied sanitation and typhoid in Chile. He reviewed previous epidemics and some 300 cases which occurred during a recent outbreak. He concludes that the mortality from gastrointestinal infections in Chile, especially in Santiago, has increased during the last three years. Several sources of infection, including possible contamination of drinking water, are present in Santiago. The main sources of infection are green vegetables, ice cream, milk products and probably also flies. An examination of 600 samples of feces of persons handling food showed that 1.7 per cent were typhoid carriers.

Detoxicating Action of Ascorbic Acid in Gold Therapy

Dr. Rogelio E. Carratalá of Buenos Aires recently conducted clinical observations and experimental research on the role of hypovitaminosis C in the development of hypersensitivity to gold therapy. The method generally used to determine hypersensitivity to gold therapy is that of making an intradermal reaction with a gold preparation. The method advised by Carratalá is more simple and reliable. It consists in making light scarifications on a small area of both arms. They should not bleed. Immediately afterward those of one arm are covered with gauze soaked in a 20 per cent sodium gold thiosulfate solution and those of the other arm are covered with gauze soaked in a mixture of this solution and a 20 per cent ascorbic acid solution. The soaked gauze on each arm is left in contact with the scarifications for fifteen to twenty hours, after which it is removed and the results are read as when an intradermal test is performed. The author made observations in 6 cases of rheumatism. The results of the reaction to the sodium gold thiosulfate alone were strongly positive in 4 cases, weakly positive in 1 case and negative in 1 case. The results of the reaction to the mixture of sodium gold thiosulfate and ascorbic acid were weakly positive in the case in which the same reaction appeared to sodium gold thiosulfate alone. In all other 5 cases the results of the reaction were negative. By testing the excretion of vitamin C in the urine it was found that the 4 subjects showing hypersensitiveness to gold therapy were suffering with hypovitaminosis C. The hypersensitive patients showed intolerance to the gold therapy. The symptoms were controlled by administration of vitamin C. One of the patients developed acute dermatosis in the course of gold therapy. The latter was discontinued, vitamin C was administered and gold therapy was again administered without further toxic effects.

The author experimented on guinea pigs and, on the basis of his results, emphasizes the value of vitamin C in preventing intolerance and the toxic effects of sodium gold thiosulfate.

Tuberculosis in Paraguay

Dr. J. M. Boettner, a professor in the Faculty of Medical Sciences of the National University of Paraguay, wrote an article in the *Anales de la Facultad de Ciencias Médicas*, January-June, 1941, in which he stated that the city of Asunción is now in a complete epidemic phase without having reached the greatest figures of massive tuberculous infection. People in the rural zones of Paraguay are in a state of pretuberculization. They will be easy victims for epidemic outbreaks when the routes of communication with other places improve. The antituberculosis campaign is well organized in the capital of the country; however, much is lacking. There should be ready one or one and one-half beds for tuberculous patients for each death from tuberculosis which is registered. The mortality for tuberculosis in Asunción is 190 deaths for each hundred thousand persons and it represents more than 10 per cent of the general mortality.

Deaths

Hubert Work ✠ Englewood, Colo., formerly Secretary of the Interior and President of the American Medical Association, died of coronary thrombosis in St. Joseph's Hospital, Denver, December 14.

Dr. Work was born in Marion Center, Pa., July 3, 1860. He studied at the Indiana State (Pa.) Normal School and Medical Department of the University of Michigan, taking his medical degree at the University of Pennsylvania in 1885. The same year he began the practice of medicine in Greeley, Colo. Later he removed to Pueblo, where he was a founder in 1896 of the Woodcroft Hospital for nervous and mental diseases, serving there for many years as physician in charge. He was also superintendent of the early Woodcroft School of Feeble Minded Children.

In 1908 Dr. Work was delegate at large for the Republican National Convention and subsequently served as chairman of the Colorado Republican State Central Committee and member of the Republican National Committee. In 1921 he became first assistant postmaster general of the United States. Then following one year's service as Postmaster General Dr. Work became Secretary of the Interior on March 5, 1923, a position he held until July 24, 1928. The following year he was chairman of the Republican National Committee. He was once a candidate for the United States Senate but was defeated by a small majority.

Throughout his long public career, Dr. Work maintained a deep active interest in medical developments. During the late eighties he was a member of the Colorado State Board of Medical Examiners. For four years he was president of the state board of health and later president of the Colorado State Medical Society. In 1906 he began his first term as a member of the House of Delegates of the American Medical Association. In 1916 he became the first chairman of the House of Delegates of the Association and later its first speaker. He was a member of the Judicial Council and in 1920 was chosen President-Elect of the Association, assuming the presidency in 1921.

HUBERT WORK, M.D., 1860-1942

Dr. Work's professional reputation was obtained as a clinician and psychiatrist. He received many honorary degrees and was a member of numerous scientific groups devoted to his specialty, serving in 1911 as president of the American Medico-Psychological Association. He was a fellow of the American College of Physicians and a member of the Central Neuropsychiatric Association and of the American Psychiatric Association. He was consulting physician to the Colorado Fuel and Iron Company Hospital and the Colorado State Insane Asylum, Pueblo. Twice he was chosen president of the Medical Veterans of the World War.

During World War I Dr. Work rendered distinguished services, acting as medical adviser of the Provost Marshal General. It was in this capacity that his diplomatic qualities were of inestimable service in correlating the work of the medical department of the army with that of the Provost Marshal General's Office. At the conclusion of the war he became a colonel in the medical reserve of the Army.

Dr. Work's death closes a long and distinguished life. He was a kindly man, endearing himself to every one by his affability, calm and reserve. He inspired cooperation and efficiency and was ever ready for usefulness with kind comment or witty repartee.

William Toy Shoemaker ✠ Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1891; specialist certified by the American Board of Ophthalmology; professor of ophthalmology and vice dean for ophthalmology at the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania; formerly clinical professor of ophthalmology at the Woman's Medical College of Pennsylvania; member of the American Ophthalmological Society, College of Physicians of Philadelphia and the Association for Research in Ophthalmology, Inc.; fellow of the American College of Surgeons; served as consultant to the Germantown, the Pennsylvania and the Woman's hospitals; consultant and honorary chief, department of ophthalmology, Lankenau Hospital, where he was formerly an assistant ophthalmologist, chief ophthalmologist and an executive medical officer; chief, department of ophthalmology, Graduate Hospital of the University of Pennsylvania; served overseas as a major during World War I; a contributor to medical textbooks, encyclopedias and medical journals; for five years editor of the *Annals of Ophthalmology;* aged 73; died, November 26, in the Graduate Hospital.

James T. Hurd, Galeton, Pa.; College of Physicians and Surgeons, Baltimore, 1885; member of the Medical Society of the State of Pennsylvania; past president of the Potter County Medical Society; for many years served on the school board of Galeton as a member of the board of health and as treasurer of the Potter County School Directors' Association; for many years bank president; in 1940 received an award from the Seventh Councilor District of the Medical Society of the State of Pennsylvania for fifty years of practice; aged 83; died, November 1, of coronary thrombosis.

William Elliott Dold, Charlottesville, Va.; University of the City of New York Medical Department, New York, 1880; member of the Medical Society of the State of New York, the American Psychiatric Association, the New York Academy of Medicine, the New York Society of Medical Jurisprudence and the New York Neurological Society; formerly medical superintendent of the River Crest Sanitarium, Long Island City; at one time physician to the Manhattan State Hospital and the psychiatric branch of the New York Hospital, New York; aged 86; died, November 9.

Arthur D. Gray ✠ Topeka, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1912; member of the American Urological Association; fellow of the American College of Surgeons; urologist, Christ's Hospital; member of the staff of Stormont and St. Francis hospitals; urologist and consultant in genitourinary diseases at the Topeka Municipal Clinic, Menninger Clinic and Sanitarium, Hillcrest Sanatorium and the Atchison, Topeka and Santa Fe Railway Hospital; aged 56; died, October 30, of coronary occlusion.

Robert Edwin Hilburn, Wichita Falls, Texas; University of Louisville (Ky.) Medical Department, 1909; member of the State Medical Association of Texas; served in the medical corps of the U. S. Army during World War I; for the past fourteen years medical examiner for the Wichita Falls area of the Civil Aeronautics Administration; aged 60; died, September 6, of heart disease at his farm home near Antelope.

Irving Emerson Sumner ✠ Brooklyn; University and Bellevue Hospital Medical College, New York, 1917; served in the medical corps of the U. S. Army during World War I; associate surgeon at the Beth Moses Hospital and adjunct surgeon at the Wyckoff Heights Hospital; aged 48; died,

November 9, in the Long Island College Hospital of thrombosis of the heart with multiple embolism.

Frank Hamlin Blackmarr ✠ Chicago; Hahnemann Medical College and Hospital, Chicago, 1897; member of the Radiological Society of North America, Inc.; on the staff of the Chicago Memorial Hospital; aged 71; died, September 16, of carcinomatosis due to carcinoma of the left middle finger.

William Byrne Brown ✠ Columbia, Mo.; Rush Medical College, Chicago, 1936; director of the division of health education at Stephens College; past president of the Boone County Medical Society; fellow of the American College of Physicians; aged 38; died suddenly, November 8, of heart disease.

Meyer Merle Cutler, Chicago; University of Illinois College of Medicine, Chicago, 1937; member of the Illinois State Medical Society; formerly house physician and resident radiologist at Michael Reese Hospital; aged 31; died, November 17, in Miami Beach, Fla., of rheumatic heart disease.

Pasquale A. Rosati, Pittsburgh; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1900; served as a captain in the Italian Army Medical Corps during World War I; aged 71; died, October 27, in the Belvedere General Hospital of endocarditis and cardiac asthma.

Herbert James Bryson, New Orleans; George Washington University School of Medicine, Washington, D. C., 1907; served as a major in the U. S. Army during World War I; aged 61; died, November 3, of generalized arteriosclerosis and arteriosclerotic heart disease.

Harry Raymond Fleming, Humboldt, Sask.; Queen's University Faculty of Medicine, Kingston, Ont., 1922; was first elected to the House of Commons at the general election in 1935 and reelected at the 1940 general election; aged 48; died suddenly, November 5.

Benjamin Levine, New York; New York Homeopathic Medical College and Flower Hospital, New York, 1920; served during World War I; aged 53; died, November 6, in the New York Polyclinic Hospital of carcinoma of the stomach with metastases to the pancreas.

Lucius Barton Leake ✠ Temple, Texas; University of Texas School of Medicine, Galveston, 1924; president of the Bell County Medical Society in 1934; for many years on the staff of the Kings Daughters Hospital; aged 45; died recently of carcinoma of the colon.

Clifford Reno Neare, East Orange, N. J.; Jefferson Medical College of Philadelphia, 1899; member of the Medical Society of New Jersey; for many years on the staff of the Orange Memorial Hospital, Orange; aged 68; died, November 9, of heart disease.

Charles William Titus, Bloomfield, N. J.; College of Physicians and Surgeons, Baltimore, 1897; served overseas during World War I; aged 66; died, November 5, in the Veterans' Administration Facility, Lyons, of diabetes mellitus and heart disease.

Clyde Amandee Noland ✠ Long Beach, Calif.; State University of Iowa College of Medicine, Iowa City, 1905; specialist certified by the American Board of Ophthalmology; aged 67; died, October 24, in the Community Hospital of septicemia.

Charles Collmar ✠ Easton, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1884; at various times a member of the city council; consulting physician to the Easton Hospital; aged 82; died, November 20, of coronary occlusion.

James Thomas Powell, Gravette, Ark.; Medico-Chirurgical College of Kansas City, Mo., 1903; member of the Arkansas Medical Society; served as health officer of Gravette; aged 79; died, October 28, of coronary thrombosis and angina pectoris.

Amos Canfield ✠ New York; Cornell University Medical College, New York, 1902; president of the Tioga County Historical Society from 1934 to 1940; aged 64; died, November 13, in Candor, N. Y., of cerebral hemorrhage.

Edward Robert Herman, Bloomington, Ill.; National Medical University, Chicago, 1906; Illinois Medical College, Chicago, 1907; served during World War I; aged 73; died, October 21, of hemiplegia and coronary sclerosis.

William Henry Follmer, Lewisburg, Pa.; Hahnemann Medical College of Philadelphia, 1882; aged 83; died, November 11, in the Evangelical Hospital of right hemiplegia, chronic degenerative endocarditis and arteriosclerosis.

Silas Sterling Stahl ✠ Franklin, Ohio; St. Louis University School of Medicine, 1905; at one time assistant in surgery at his alma mater; served during World War I; aged 73; died, November 6, of carcinoma of the liver.

Carl V. Urbom, Rockford, Ill.; Hering Medical College, Chicago, 1903; member of the Illinois State Medical Society; aged 83; died, October 30, in St. Anthony's Hospital as the result of a fractured hip received in a fall.

Robert Dwyer, Indianapolis; Indiana University School of Medicine, Indianapolis, 1908; member of the Indiana State Medical Association; aged 64; died, November 11, in St. Francis Hospital of cerebral hemorrhage.

William Josiah Shipp, Ore City, Texas; College of Physicians and Surgeons, Dallas, 1906; St. Louis College of Physicians and Surgeons, 1908; aged 65; died, October 16, in a hospital in Dallas of uremia.

Thomas Arthur Costello, Cleveland; University of Wooster Medical Department, Cleveland, 1900; served in the medical corps of the U. S. Army during World War I; aged 69; died, October 15.

Mary Ladd Bruner, Greenfield, Ind.; Woman's Medical College, Chicago, 1885; for many years a trustee at Earlham College, Richmond, Ind.; aged 87; died, November 6, of chronic arthritis.

Wade Hampton Atkinson ✠ Washington, D. C.; Georgetown University School of Medicine, Washington, 1889; aged 76; died, November 14, in Johnston County, N. C., of angina pectoris.

Mina Logue Fuller Peterson Brainard, Avalon, Calif.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1879; aged 86; died, October 17, of heart disease.

Joseph Lane Voorhies, Columbia, Tenn.; College of Physicians and Surgeons, Baltimore, 1886; formerly health officer of Maury County; aged 82; died, October 24, of heart disease.

Charles R. Tanner, Henderson, Ky.; University of Tennessee Medical Department, Nashville, 1901; aged 65; died, November 2, in the Henderson Hospital of myocarditis.

Daniel Emmett Barnett, Homer, Ind.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1905; aged 67; died, November 18, of coronary occlusion.

Clarence S. Bolender, Clearwater, Fla.; Eclectic Medical College of Indiana, Indianapolis, 1903; aged 80; died, November 6, of congestive heart disease and senility.

Robert Lee Jenkins, Winston-Salem, N. C.; College of Physicians and Surgeons, Baltimore, 1903; aged 71; died, November 1, of coronary thrombosis.

Mysta L. Austin Hendricks, Salem, Ore.; Willamette University Medical Department, Salem, 1907; aged 61; died, October 29, of heart disease.

Quincy A. Sturgeon, Madrid, Iowa; Kentucky School of Medicine, Louisville, 1883; aged 83; died, October 24, of myocarditis and hypertension.

Jewel Holt Vaught, Chicago; Central College of Physicians and Surgeons, Indianapolis, 1903; aged 68; died, October 30, in Williamsfield, Ill.

Joseph David Franklin Dove, St. Joseph, Mo.; Rush Medical College, Chicago, 1888; aged 76; died, November 10, of coronary occlusion.

Hilliard Neil A. McLean, Detroit; Detroit College of Medicine, 1899; aged 67; died, September 18, at his home in Farmington, Mich.

Helen Gyori, New York; Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1902; died, November 6.

Adelbert Beeman Allen ✠ Richmond, Maine; University of Vermont College of Medicine, Burlington, 1904; aged 63; died, October 8.

Roy Armstrong Bond, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1915; aged 59; died, November 9.

DIED WHILE IN MILITARY SERVICE

Vincent Giuliano Maggiore, Brooklyn; University of Virginia Department of Medicine, Charlottesville, 1928; captain in the medical corps of the Army of the United States, attached to Company D, 7th Medical Battalion, Camp San Luis Obispo, California; began active duty Aug. 8, 1942; aged 38; was killed in a railroad accident at Casmalia, Calif., December 5.

Bureau of Investigation

STIPULATIONS

Agreements Between Federal Trade Commission and Promoters of Various Products

The following items are abstracts of stipulations in which promoters of "patent medicines," medical devices and cosmetics have cooperated with the Federal Trade Commission to the extent of agreeing to discontinue certain misrepresentations in their advertising. These stipulations differ from the "Cease and Desist Orders" of the Commission in that such orders definitely direct the discontinuance of misrepresentations. The abstracts that follow are presented primarily to illustrate the effects of the provisions of the Wheeler-Lea Amendment to the Federal Trade Commission Act on the promotion of such products.

Besol.—This is put out by Besol, Inc., Cleveland, as a treatment for the paroxysms of asthma. In July 1942 that concern signed a stipulation with the Federal Trade Commission in which it agreed to discontinue any advertisements which failed to reveal that its product should not be used by persons suffering from high blood pressure, heart disease, diabetes, thyroid, goiter, lung disorders or skin rash and that the prescribed dosage should be diminished or use of the products discontinued if sleeplessness or nervousness should develop. It was provided, however, that the advertisements need contain only the statement, "Caution: Use only as directed," if the directions for use in the labeling contains a warning to the same effect.

Chamberlain's Lotion.—In August 1942 the Chamberlain Sales Corporation and its President, L. H. Chamberlain, Des Moines, Iowa, stipulated with the Federal Trade Commission that they would cease representing that any test made to show that "Chamberlain's Lotion" flows more readily than other lotion indicates that it is superior to others, or that other lotions containing tragacanth gum or other filler are sticky. Chamberlain's Lotion was mentioned in an earlier stipulation signed with the Commission in December 1936 by a Des Moines concern, then known as Chamberlain Laboratories, in which it agreed to cease representing in advertisements that Chamberlain's Lotion will revitalize the skin and enable it to retain the radiance of youth; that it is a complete beauty treatment containing a blend of thirteen imported oils, each of which is noted for a specific skin need; that it will prevent sunburn, windburn and cracked, irritated skin in all cases and that it is a competent treatment for athlete's foot.

Floting Oil-of-Castor.—This is a permanent wave solution put out by B. E. Sanders, Inc., Tulsa, Okla. In July 1942 that concern stipulated with the Federal Trade Commission that it would cease representing that its product is a new type of permanent wave solution and will nourish the hair, or that it contains less ammonia than that found in other solutions used for the same purpose. The Sanders firm further agreed to cease representing that its preparation is sold by means of a special introductory or limited offer and, by use of the words "'Floting Oil-of-Castor," that the oil ingredient is composed principally of castor oil.

Hemorointment.—This is put out by a Frank Hill, trading as Hill Laboratories, Carterville, Ill. In July 1942 Hill stipulated with the Federal Trade Commission that he would cease representing that his product is a remedy for the healing or cure of hemorrhoids or that it contains no harmful ingredients or is guaranteed, unless the terms of the guaranty are fully set forth. Further, Hill agreed to drop the use of the word "Laboratories" in his trade name and to cease representing in any other way that he owns, operates or controls a laboratory.

Henry Yee Herb Company.—Under this trade name one Yee Why, also known as Henry W. Yee, of Sacramento, Calif., sold herbs for the treatment of various diseases. In a stipulation that he signed with the Federal Trade Commission in August 1942 he agreed to cease representing by means of advertisements sent through the mail, radio broadcasts or other media that his herbs can be depended on to purify the blood or impart normal, healthy tone to the body or that they constitute a competent treatment or effective remedy for nerve symptoms or pains, nervousness, neuritis, rheumatism, liver or kidney disorders, cancer of the bowels, heart trouble, anemia or other ailments.

Kema Tablets and Kema Tea.—These are sold by one Harry C. House, trading as Western Natural Foods Company, Seattle. In July 1942 House signed a stipulation with the Federal Trade Commission in which he agreed to discontinue these misrepresentations: that either of his products has value as a weight reducer or an accessory or supplemental food or dietary aid or has any significant food value; that either one supplies mineral colloids essential to hydrolysis, saponification, oxidation or elimination of fat; that "Kema Tea" keeps organs of elimination in proper working order or that either product is harmless. House further stipulated that he would discontinue any advertisements which failed to reveal that his preparations should not be used when abdominal pain, nausea or other symptoms of appendicitis are present, or that frequent or continued use of his products may result in dependence on laxatives; provided, however, that such advertisements need contain only the statement, "Caution: Use only as directed," if and when the label contains directions which include a warning to the same effect.

Makasar Wonderful Pomade and Makasar Wonderful Pomade Double Strength.—These were represented as having value in treating conditions which cause falling hair, by Mack Jenious and Gensie Jenious, trading as Makasar Beauty Products Company and Mme. Gensie Jenious and Company, Montclair, N. J. In a stipulation that these persons signed with the Federal Trade Commission in August 1942 they agreed to discontinue such misrepresentation.

Minra.—This is a product of the Stayner Corporation, San Francisco, whose advertising is handled by an agency in the same city known as Erwin Wasey and Company of the Pacific Coast. In August 1942 this agency signed a stipulation with the Federal Trade Commission agreeing to discontinue any advertising which represented, among other things, that Minra is a remedy or cure for acidosis, indigestion, influenza, infection, headaches, or toxemia; that it furnishes the necessary materials to produce sound teeth, bones, muscles or good health or gives protection against mineral deficiencies, or that any of the results claimed for the product have been proved by tests made at universities or colleges, or by competent trainers or coaches, or on college athletes.

Naturene.—In July 1942 the Swiss Pine Importing Company, Inc., New York, stipulated with the Federal Trade Commission that it would cease advertising that this hair dye restores the original or natural color of the hair, is harmless and does not stain the scalp. The company further agreed to discontinue any advertisements which failed to reveal that "Naturene" contains a metallic salt and hence must be used with care. The stipulation provided, however, that it would be sufficient for the advertisements to state, "Caution: Use only as directed," if and when the directions for use, wherever they appear in the labeling, contain a warning to the same effect.

Pelmanism.—This system, also designated "Pelman Institute's Complete Course of Correspondence Instruction in Scientific Mind Training," is promoted by the Pelman Institute of America, Inc., New Rochelle, N. Y. In July 1942 that concern stipulated with the Federal Trade Commission that it would cease using the word "Institute" as part of its corporate or trade name or in any other manner so as to imply that its correspondence school is conducted for the promotion of learning, such as philosophy, art or science, or has equipment and a faculty such as to entitle it to be designated an "institute"; would discontinue representing that its home study course in mind training, also known as "Pelmanism," trains the mind as a physical instructor trains the body; develops character, helps to make friends or opens the way to honor, wealth or happiness; increases energy or enlarges capacities for enjoyment; shows how to banish forgetfulness, brain fag, indecision, self consciousness, or lack of ideas; teaches one how to acquire a keen or infallible memory or a masterful personality, and can be depended on to cause students to attain financial, social and intellectual success. The concern further agreed to cease representing that Pelmanism is endorsed by the world's leading educators; that it has offices in various foreign cities, that its correspondence school has a staff of trained psychologists or a faculty of instructors, or that students receive personal instruction.

Pixacol.—This is sold by one Bernard Singerman, trading as Pixacol Company, Cleveland. In September 1942 he signed a stipulation with the Federal Trade Commission in which he agreed to cease representing that his product is a cure for psoriasis. He further agreed to discontinue any advertisements which failed to reveal that "Pixacol" may irritate the skin, particularly if applied with rubbing; that the user should avoid getting it into his eyes or on mucous membranes and that it should in no case be applied to large areas of the body. The stipulation provided, however, that it would be sufficient for the advertisement simply to state, "Caution: Use only as directed," when the directions on the labeling contain a warning to the same effect.

S. C. S. Corn Salve and S. C. S. Athlete's Foot Salve.—These products are sold by Anton and Oldrich Sebeck, operating as S. C. S. Chemical Company, Chicago. In September 1942 these persons stipulated with the Federal Trade Commission that they would discontinue the following misrepresentations: that the corn salve is a remedy or cure for corns or will enable one to get rid of them or is a remedy or cure for calluses or warts; that the foot salve will cure athlete's foot or ringworm or effectively treat those conditions, unless such claims are limited to cases which are not deep seated; or that the foot salve is effective in the treatment of eczema. The Sebecks further stipulated that in the sale of the foot salve or any product of similar composition it would not disseminate any advertisements which fail to reveal that it should not be applied to extensive areas of the body or used continuously for an extended period and that its use should be discontinued if a skin irritation appears; and that they would cease issuing any advertisements of "S. C. S. Corn Salve" which did not include the warning that it should not be applied to sores, ulcerations, open wounds or any area of the body other than that under treatment. The stipulation provided, however, that advertisements of either preparation need contain only the statement, "Caution: Use only as directed," if the directions for use on the labels contain a warning to the same effect.

Sun-Ra Vitamin Ointment.—In a stipulation signed in July 1942 with the Federal Trade Commission by a John A. Muise and an Arthur S. Ryan, doing business as Sun-Ra Company, Gloucester, Mass., these persons agreed to cease representing that their product is a remedy, treatment or cure for eczema or is of any value in treating psoriasis, insect bites, abrasions or skin irritations beyond having a limited value in the treatment of bites of nonvenomous insects and in the relief of minor abrasions and skin irritations; that the preparation is healing or contains boric acid or has no harmful ingredients. Muise and Ryan further agreed to cease using the word "Vitamin" as part of the brand name for their product or otherwise representing that it has any merit by reason of any vitamins that it may contain.

Correspondence

TRAUMA AND CORONARY OCCLUSION

To the Editor:—In the October 3 issue of THE JOURNAL on page 392, Master took issue with your editorial quotation of my paper (Sigler, L. H.: Trauma of the Heart Due to Nonpenetrating Chest Injuries, THE JOURNAL, July 11, 1942, p. 855) that trauma can produce coronary occlusion.

It was not my intention in the paper cited to show that trauma may produce merely coronary occlusion, although no one has as yet disproved such a possibility. My purpose was to demonstrate that trauma of the heart may be caused by nonpenetrating injuries to the chest and other parts of the body.

If myocardial infarction develops, and that I have definitely demonstrated in those cases in which I claim that it had occurred, it is immaterial whether the infarction was induced through the intermediation of coronary occlusion or by direct injury to the heart muscle. The very recognition of coronary occlusion is by the myocardial infarction it produces. In the absence of demonstrable infarction after an assumed attack of coronary occlusion we must question the correctness of the diagnosis, although coronary occlusion might occur without infarction in a small percentage of cases. Myocardial infarction may occur without complete structural coronary occlusion as seen on postmortem examination. In such cases it is due presumably to prolonged coronary spasm during life or to sudden strain thrown on a heart which has a poor coronary blood supply.

We cannot entirely agree with Master's statement that "coronary occlusion (coronary thrombosis) . . . is a complete closure of a coronary artery, with massive confluent, through and through infarction as a rule." The amount of infarction caused by coronary occlusion varies directly with the size of the artery occluded and inversely with the extent of the collateral circulation. Any size and variety of infarction may be observed even in occlusion of the same vessel in different individuals. We also must not mix up the terms "coronary occlusion" and "coronary thrombosis." Whereas the latter invariably implies coronary occlusion, the former may represent a closure of a vessel by any other process than thrombosis. For instance, capillary hemorrhage in the vessel wall may occur in sufficient degree to occlude the lumen of the vessel, as was recently shown by Wartman and by Patterson. Also the rupture of a so-called atheromatous "abscess" may produce occlusion, as suggested by Leary. In such cases intravascular thrombosis may supervene, but the primary process is not thrombosis. Some such process may occur in a vessel in trauma of the heart or as a result of severe strain. However, whether or not this occurs is irrelevant as long as we can demonstrate the presence of myocardial infarction or other traumatic changes after an injury.

Patient 4 of my paper which Master selected for criticism was not seen by me until four weeks after the accident. The patient was treated in some hospital, which reported to me that he showed evidence of coronary thrombosis soon after the accident. It is for that reason that I could not present more detail of the early phases of the disease. The subsequent course and electrocardiographic changes together with the history, however, speak for themselves.

It is unfortunate that we have been considering the problem of traumatic injury to the heart from the narrow point of view of the occurrence of coronary thrombosis and not of trauma to the heart as a whole. Pro and con opinions have been rendered in the same case by cardiologists, based on insufficient experience and on improper investigation of the field in the past. The cardiovascular changes in few cases of bodily injuries have been studied soon after an accident, and the profession is simply ignorant of the frequency of occurrence and the extent of traumatic injuries to the heart.

A good start in the proper direction of investigation of this problem has recently been made by Barber (Hugh: Electrocardiographic Changes Due to Trauma, *Brit. Heart J.* **4**:83 [July] 1942). He found abnormal electrocardiographic changes in 8 out of 33 accident cases in which studies were made within the first few days after an accident.

LOUIS H. SIGLER, M.D., Brooklyn.

THE KENNY TREATMENT IN INFANTILE PARALYSIS

To the Editor:—Dr. McCarroll in THE JOURNAL, October 17, states that he feels sure the Kenny method of treatment for the disease infantile paralysis would in time take its place among the others offered by the field of physical therapy as having been tried but found wanting.

The application of physical therapy in the past was for symptoms that did not exist and, consequently, the results could not have been satisfactory. I am not referring to the pathology of the disease but to the symptomatology.

The symptomatology accepted by Dr. McCarroll, for which physical therapy has had no response—in fact, according to his investigation, has proved damaging—is that previously accepted throughout the world. It may be explained by an extract from Public Health Bulletin No. 242, presented to me by the National Foundation for Infantile Paralysis on my arrival in the United States of America:

> The damaged nerve cells are in the cord inaccessible to any form of treatment, their recovery being based on the character and degree of injury they have sustained. At this point appears the importance of the muscle, a tissue in no way directly attacked by the virus but rendered as useless by its loss of innervation as an automobile with its battery stolen. The muscle undergoes certain degenerative changes, the most important of which is its loss of tone or state of tension, so that instead of being taut and elastic it is relaxed, easily stretched and sagging like a hammock between its points of origin and insertion.

The result of treatment by physical therapy as it is practiced throughout the world is presented by Dr. McCarroll in (1) the *Journal of Bone and Joint Surgery*, October 1941, and (2) THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, October 17, and reads:

	Percentage of Normal Recoveries
Group 1.	
Immobilization 1 to 4 months.	
No physical therapy	9
Group 2.	
Immobilization 1 to 3 months.	
Physical therapy 3 to 6 months	0
Group 3.	
Immobilization 4 to 18 months.	
No physical therapy	2
Group 4.	
Immobilization 3 to 12 months.	
Physical therapy 8 to 24 months	13
Group 5.	
No treatment	17

It will be seen by this statement that physical therapy, as it is practiced, not only failed to achieve results but prevented recovery in a certain percentage of cases.

The Kenny concept of the symptomatology (which is just the opposite to that already quoted) first appeared in THE JOURNAL, June 7, 1941. This concept appeared in the report of my work presented by Dr. Wallace Cole, professor of orthopedic surgery, and Dr. Miland Knapp, professor of physical therapy, University of Minnesota Medical School, and reads:

> Miss Kenny has presented ideas which are new to us in the symptomatology and treatment of infantile paralysis. . . . According to this concept the cardinal symptoms of infantile paralysis are, to use her terms, muscle spasm, muscle incoordination and mental alienation. This is opposed to the usual concept where the cardinal symptom is flaccid paralysis without spasm or incoordination. The presence of spasm has been demonstrated in 100 per cent of the acute cases observed in this study.

The results of the treatment given for this concept also appeared in (1) the report mentioned and states that there were 55 per cent recoveries to normal in 32.6 days, and (2) the records

of the Orthopedic Hospital, New York, presented to the medical observers of the work at the University of Minnesota and myself by Dr. Robert Bingham in June 1942, and reads:

I. "Orthodox Treatment"—absolute bed rest with immobilization by means of splints or plaster casts and shells for protection of weak and paralyzed muscles, prevention of and correction of deformities, and physical therapy and muscle training.

II. "Orthodox plus Kenny Treatment"—substitution of the Kenny methods on patients who had received the classical treatment at onset of their illness and for some period of time.

III. "Kenny Treatment"—for symptoms in the acute stage: bed rest and hot moist formentations for muscle spasm, passive motion to restore awareness in mental alienation, and muscle reeducation for muscle incoordination and recovery of muscle power.

The average duration of hospitalization in the three groups:

Group I. 16 months
Group II. 9 months
Group III. 6 months

Estimated results of treatment:

	"Orthodox Treatment" 12 Patients	"Orthodox Plus Kenny" 24 Patients	"Kenny Treatment" 24 Patients
Patients with residual paralysis (muscle groups fair or less)...	10 87%	14 58%	8 33%
Number of braces needed (some patients use several).....	19 braces	10 braces	6 braces
Patients needing braces or surgery	6 50%	8 33%(?)	4 16%(?)
Patients with deformities.....	9 75%	6 25%(?)	2 8%(?)
Functional result: Excellent	1	6	11
Good	3	8	10
Fair	4	7	3
Poor	4	3	0

The results obtained by physical therapy taught at the University of Minnesota and the City Hospital, Minneapolis, for the true symptoms of this disease speak for themselves and need no comment from me.

The evidence presented in this communication is not my own but supplied by physicians. The slides presented by Dr. McCarroll throughout the state of Missouri and elsewhere, presenting certain patients treated at the Gillette State Hospital, were not patients who had received the Kenny treatment.

ELIZABETH KENNY, Minneapolis.

PREMEDICAL EDUCATION

To the Editor:—The urgency of the need for military physicians has revived discussion concerning the length of time a student must spend in premedical education. A rigid requirement of four years and a degree for entrance in a medical school is unnecessary and unwise. I do not believe that the average medical student who was obliged to spend four years in academic work is superior enough to those who have not to justify the expense in money and years. While it may be desired and even urged for the student who is exceptionally receptive, young and well financed, many students unfortunately have neither the ambition nor the ability to absorb the kind of education they are exposed to, regardless of their financial backing. Nor does the average student need a prolonged classical education to become a good doctor. If a student does not or cannot acquire "culture" during or after his professional education, there is little likelihood that he will obtain it by forced requirements of years, credits or degrees in colleges. Furthermore, baccalaureate degrees in many cases have lost their prestige through mass production, so that they are now often mere tags of educational processing and not the rewards for scholarly attainment for which they were originally intended.

This is not the place to discuss the faults or shortcomings of the organization for primary and secondary education or to offer suggestions for its improvement. Neither is there need to recall how old the average medical student is under the present system before he is able to practice. It would seem that for the majority of students one year or, at most, two years of premedical education as a minimum admission requirement should suffice, or perhaps the medical course itself could be expanded to include certain preliminary subjects. As it is, the extra years now demanded for entrance requirement by many medical schools could better be spent in postgraduate work or other medical pursuits for the student who is intellectually receptive, and "culture" will or should accrue with them, with or without extra degrees.

HOBART A. REIMANN, M.D., Philadelphia.

THE DOCTOR IN POLITICS

To the Editor:—To a second year medical student the comments of Sir Beckwith Whitehouse on the ominous signs appearing in the rising generation of doctors (which you reprinted in the issue of November 7, page 754) were most interesting. Sir Beckwith decried (i) a growing interest in purely materialistic financial success and (ii) a growing interest in assuming active political roles. He disapproved on the grounds that they represented a departure from attention to the doctor's primary avowed concern—the welfare of humanity.

These two interests are not the same. It would rather seem that the more the doctor cares about his job and the more thoroughly he thinks it through, the more ardent a politician he must become. Surely it has been through political activity that some of his most cherished ends have been achieved—compulsory vaccination, regulation of water, milk and food, negative serologic reaction of prospective mates, and so on. But the doctor is also concerned with politics in a broader sense, for example as it affects his patients economically and socially. It is tragic for him to be unable to help one of them because of a far gone malignant growth or because of a constitutional inadequacy; it is almost as tragic to perform a perfect gastrojejunostomy for a patient who has very little to live for once he leaves the hospital.

The scientists of Germany performed the greatest disservice to their country through their aloofness to the political arena and through their clinging to purely technical concerns. It is for the doctor not to disdain political interest but rather to cultivate it: because, if politics go badly, his private labors for humanity are pitifully ineffectual; but, if they go well, he is assisted by preventive medicine at its best.

So perhaps Sir Beckwith should cheer up!

NICHOLAS S. GIMBEL,
University of Pennsylvania School of Medicine,
Philadelphia.

BURNS FROM RUBBER SOAKED IN CRESOL

To the Editor:—Perhaps attention should be called to an item under "How to Conserve Medical and Surgical Rubber Goods" on page 847 of the November 14 issue of THE JOURNAL. Referring to the care of rubber tubing, the following statement occurs: "Stomach tubes should be rinsed and thoroughly cleansed and then soaked in 5 per cent solution of cresol for one hour." Small tubes for stomach drainage are often left in place for many hours or days. Injury of the mucous membrane from contact of these tubes has been reported. It is pertinent, therefore, to call attention to the absorption of cresol by rubber. "Burns" of the skin through contact with rubber previously soaked in cresol have been reported (Herwick, R. P., and Treweek, D. N.: Burns from Anesthesia Mask Sterilized in Compound Solution of Cresol, THE JOURNAL, Feb. 11, 1933, p. 407).

RALPH M. WATERS, M.D., Madison, Wis.
Department of Anesthesia, State of
Wisconsin General Hospital.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

CHICAGO, Feb. 15-16, 1943. Sec., Council on Medical Education and Hospitals, Dr. H. G. Weiskotten, 535 North Dearborn Street, Chicago.

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Dec. 12, page 1244.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, Jan. 20-22 and March 1-3. Part III. Chicago, Jan. 5-7. Exec. Sec., Mr. Everett S. Elwood, 225 S. Fifteenth St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Feb. 15. Final date for filing application is Jan. 1. Asst. Sec., Dr. William A. Werrell, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Various centers, Feb. 13. Candidates in military service may take Part I at their place of duty. *Oral. Part II.* Pittsburgh, May 19-25. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* June. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* New York, May or June. Final date for filing application is March 1. Sec., Dr. Dean M. Lierle, 1500 Medical Arts Bldg., Omaha, Neb.

AMERICAN BOARD OF PEDIATRICS: *Oral.* New York, April 24-25. Final date for filing application is Jan. 1. Starting July 1, 1943, Group I will be abolished. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY & NEUROLOGY: Detroit, prior to the meeting of the American Psychiatric Association. Final date for filing application is March 1. Sec., Dr. Walter Freeman, 1028 Connecticut Ave., N.W., Washington, D. C.

AMERICAN BOARD OF SURGERY: Part I. March 4. Final date for filing application is Jan. 25. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 12-14. Sec., Dr. Gilbert J. Thomas, 1409 Willow St., Minneapolis.

Maryland June Report

The Board of Medical Examiners of Maryland reports the written examination for medical licensure held at Baltimore, June 9-12, 1942. The examination covered 9 subjects and included 90 questions. An average of 75 per cent was required to pass. One hundred and thirty candidates were examined, 126 of whom passed and 4 failed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
College of Medical Evangelists		(1942)	1
George Washington University School of Medicine		(1941), (1942)	2
Georgetown University School of Medicine		(1941, 2), (1942)	3
Howard University College of Medicine		(1936)	1
Rush Medical College		(1940)	1
Johns Hopkins University School of Medicine		(1916), (1928), (1936), (1941, 2), (1942, 47)	52
University of Maryland School of Medicine and College of Physicians and Surgeons		(1940), (1941), (1942, 59)	61
Harvard Medical School		(1939)	1
University of Pennsylvania School of Medicine		(1941)	1
Hamburgische Universität Medizinische Fakultät		(1930)	1
Medizinische Fakultät der Universität Wien		(1938)	1
Universität Heidelberg Medizinische Fakultät		(1926)	1

School	FAILED	Year Grad.	Number Failed
Georgetown University School of Medicine		(1941)	1
University of Maryland School of Medicine and College of Physicians and Surgeons		(1942)	1
Hamburgische Universität Medizinische Fakultät		(1921)	1
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest		(1914)	1

Colorado Endorsement Report

The Colorado State Board of Medical Examiners reports 5 physicians licensed to practice medicine by endorsement on Oct. 6, 1942. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Rush Medical College		(1938)	Illinois
University of Chicago, The School of Medicine		(1940)	Illinois
State University of Iowa College of Medicine		(1925)	Iowa
Creighton University School of Medicine		(1935)	California
University of Wisconsin Medical School		(1941)	Wisconsin

Utah June Report

The Utah Medical Examining Board reports the written examination for medical licensure held at Salt Lake City, June 24, 1942. The examination covered 11 subjects and included 55 questions. An average of 75 per cent was required to pass. Fourteen candidates were examined, all of whom passed. Nine physicians were licensed to practice medicine by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Stanford University School of Medicine		(1942)*	1
University of Colorado School of Medicine		(1941), (1942)*	2
Northwestern University Medical School		(1942), (1942)†	2
Rush Medical College		(1941, 4)	4
University of Illinois College of Medicine		(1941)	1
University of Louisville School of Medicine		(1942)*	1
University of Maryland School of Medicine and College of Physicians and Surgeons		(1941)	1
Harvard Medical School		(1942)*	1
Temple University School of Medicine		(1941)	1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Colorado School of Medicine		(1941)	Colorado
Northwestern University Medical School		(1941)	Illinois
Rush Medical College		(1929), (1939)	Illinois
University of Illinois College of Medicine		(1939)	Illinois
Universtiy of Michigan Department of Medicine		(1908)	Michigan
Washington University School of Medicine		(1936), (1939)	Missouri
Columbia University College of Physicians and Surgeons		(1917)	New York

* Licenses have not been issued.

† This applicant received the M.B. degree and will receive the M.D. degree on completion of internship. Licenses have not been issued.

Louisiana June Report

The Louisiana State Board of Medical Examiners reports the written examination for medical licensure held at New Orleans, June 4-6, 1942. The examination covered 12 subjects and included 100 questions. An average of 75 per cent was required to pass. Ninety-two candidates were examined, all of whom passed. Three physicians were licensed to practice medicine by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
University of Colorado School of Medicine		(1941)	1
Yale University School of Medicine		(1941)	1
George Washington University School of Medicine		(1941)	1
Loyola University School of Medicine		(1942)	1
Northwestern University Medical School		(1940), (1942)	2
Rush Medical College		(1941)	1
University of Chicago, The School of Medicine		(1941, 2)	2
Louisiana State University School of Medicine		(1942, 3)	3
Tulane University of Louisiana School of Medicine		(1942, 76)	76
University of Michigan Medical School		(1941)	1
University of Rochester School of Medicine and Dentistry		(1941)	1
Jefferson Medical College of Philadelphia		(1941)	1
University of Wisconsin Medical School		(1941)	1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Tulane University of Louisiana School of Medicine		(1936), (1939)	Mississippi
Baylor University College of Medicine		(1936)	Texas

Georgia October Report

The Georgia State Board of Medical Examiners reports the written examination for medical licensure held at Atlanta, Oct. 12-13, 1942. The examination covered 10 subjects and included 100 questions. An average of 80 per cent was required to pass. Two candidates were examined and passed. Five physicians were licensed to practice medicine by reciprocity and 2 physicians so licensed on endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Northwestern University Medical School		(1939)	1
Wayne University College of Medicine		(1936)	1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Emory University School of Medicine		(1938)	Michigan
Duke University School of Medicine		(1940)	N. Carolina
Temple University School of Medicine		(1934)	N. Carolina
Medical College of the State of South Carolina		(1930)	S. Carolina
University College of Medicine, Richmond		(1913)	Dist. Colum.

School	LICENSED BY ENDORSEMENT	Year Grad.
Harvard Medical School		(1933)
McGill University Faculty of Medicine		(1933)

Arizona October Report

The Arizona State Board of Medical Examiners reports the written examination for medical licensure held at Phoenix, Oct. 6-7, 1942. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. One candidate was examined and passed. Six physicians were licensed to practice medicine by reciprocity and 1 physician was licensed on endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Columbia University College of Physicians and Surgeons		(1940)	1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Loyola University School of Medicine		(1930)	Illinois
Northwestern University Medical School		(1938)	Illinois
Indiana University School of Medicine		(1938)	Indiana
Washington University School of Medicine		(1937)	N. Carolina
Jefferson Medical College of Philadelphia		(1923)	Penna.
University of Toronto Faculty of Medicine		(1932)	Maryland

School	LICENSED BY ENDORSEMENT	Year Grad.
McGill University Faculty of Medicine		(1937)

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Contraceptives: Unlawful for a Physician to Prescribe or Advise Use.—A Connecticut statute forbids the use by any person of any drug, medicinal article or instrument for the purpose of preventing conception and declares it unlawful for any one to assist, abet or counsel another to commit such an offense. In *State* v. *Nelson*, 126 Conn. 412, 11 A. (2d) 856, J. A. M. A. **115**:962 (Sept. 14) 1940, it was held that no exception to this statute could be implied in favor of a physician even when in his opinion the "general health" of a married woman required the use of contraceptives. In the present case a licensed physician brought an action for a declaratory judgment to determine whether or not he could prescribe the use of contraceptive devices for married women patients (*a*) when the patient suffers from high blood pressure so that if pregnancy occurred there would be imminent danger of toxemia of pregnancy which would have a 25 per cent chance of killing her; (*b*) when the patient suffers from an arrested case of tuberculosis of such a type that pregnancy might reactivate the disease and set back her recovery for several years and might result in her death, and (*c*) when the patient, though in good health, has been weakened by having had three pregnancies in about twenty-seven months and another pregnancy would probably have a serious effect on her general health and might result in permanent disability. The action was filed in the superior court but was reserved by that court for the advice of the Supreme Court of Errors of Connecticut.

The plaintiff's first claim was that the statute, having been originally enacted in 1879 as part of a law against obscenity, had no reference to the medical situation here presented. It was sufficient to point out, said the court, that the statute contained three prohibitions. One was directed against obscene pictures and literature; a second forbade the use of any drug, medicine, article or instrument whatever for the purpose of preventing conception, and a third, the use of such articles for the purpose of causing unlawful abortion. The latter two stamp the statute as having far wider scope than mere general obscenity. To the plaintiff's argument that the legislative history of the statute had no significance, the court pointed out that this claim had been discussed and rejected in the Nelson case, in which consideration was given in detail to the repeated and recent refusals of the legislature to inject an exception. Since that decision a so-called medical birth control bill failed of enactment in the 1941 General Assembly. The result of all the attempts to secure a change is that none was made. Year after year there was ample opportunity for the legislature to create an exception in cases in which life might be in jeopardy if pregnancy occurred. Its refusal impelled the conclusion that not even in such situations as are presented in the present case did the legislature wish to permit exceptions.

The plaintiff contended further that if the statute be construed according to its express language it would violate the state and federal constitutions. But, pointed out the court, the Supreme Court of the United States has held to the contrary in the case of *Commonwealth* v. *Gardner*, 300 Mass. 372, 15 N. E. (2d) 222, 305 U. S. 559, 59 S. Ct. 90, J. A. M. A. **112**:576 (Feb. 11) 1939. In that case the Massachusetts court said, in substance, that the terms of the statute were plain, unequivocal and peremptory and contained no exceptions; that the statute was originally enacted in 1879 (as was the Connecuticut law); that under the police power the legislature, without any denial of rights under either the state or the federal constitution, might take the view that the use of contraceptives would not only promote sexual immorality but would expose the commonwealth to other grave dangers, and that prevention of conception by medical advice and treatment was not unknown in 1879 and might have been the subject of an exception from the general legislative prohibition if the legislature had deemed such an exception consonant with public policy. An attempt was made to have the decision in the Gardner case reviewed by the Supreme Court of the United States, but the defendant's appeals were summarily dismissed "for want of a federal question."

The use of contraceptives, said the court in the present case, is not the only method for preventing conception. There is another method, positive and certain in result—abstention from intercourse. If there is one remedy, reasonable, efficacious and practicable, it cannot fairly be said that the failure of the legislature to include another reasonable remedy is so absurd or unreasonable that it must be presumed to have intended the other remedy also. The legislature is the final forum. When the law it enacts comes to the courts, an implied limitation on the operation of the statute may be made only in recognition of long existing and generally accepted rights or to avoid consequences so absurd or unreasonable that the legislature must be presumed not to have intended them. Birth control is a highly controversial subject. Social thinking is divergent. It finds frequent expression at legislative hearings. Then the legislature speaks. In the statute involved in this case, the court said, the legislature has infringed on what a large body of intelligent citizens believe are their natural rights and privileges. The answer is that "The possession and enjoyment of all rights are subject to such reasonable conditions as may be deemed by the governing authority . . . essential to the safety, health, peace, good order, and morals of the community." In the opinion of the court, the statute prohibits the action proposed to be done by the plaintiff under the circumstances disclosed in his complaint and that statute is constitutional.—*Tileston v. Ullman, State's Attorney, 26 A. (2d) 582 (Conn., 1942).*

Society Proceedings

COMING MEETINGS

Annual Congress on Industrial Health, Chicago, Jan. 11-13. Dr. Carl M. Peterson, 535 North Dearborn St., Chicago, Secretary.

American Academy of Orthopaedic Surgeons, Chicago, Jan. 17-21. Dr. Myron O. Henry, 825 Nicollet Ave., Minneapolis, Acting Secretary.

Annual Forum on Allergy, Cleveland, Jan. 9-10. Dr. Jonathan Forman, 956 Bryden Road, Columbus, Ohio.

Clinical Orthopaedic Society, Chicago, Jan. 18-21. Dr. Myron O. Henry, 825 Nicollet Ave., Minneapolis, Secretary.

Eastern Section, American Laryngological, Rhinological and Otological Society, Hartford, Conn., Jan. 15. Dr. Edward J. Whalen, 750 Main St., Hartford, Conn., Chairman.

Middle Section, American Laryngological, Rhinological and Otological Society, Detroit, Jan. 20. Dr. Voss Harrell, 2539 Woodward Ave., Detroit, Chairman.

Southern Section, American Laryngological, Rhinological and Otological Society, Chattanooga, Tenn., Jan. 28. Dr. Francis B. Blackmar, 1301 Broadway, Columbus, Ohio, Chairman.

Western Section, American Laryngological, Rhinological and Otological Society, Portland, Ore., Jan. 31. Dr. Irving M. Lupton, 1020 S.W. Taylor St., Portland, Ore., Chairman.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

64:585-770 (Oct.) 1942

Anxieties of Children: Their Causes and Implications. B. I. Beverly, Chicago.—p. 585.
*Concomitance of Chronic Acidosis with Late Rickets. J. D. Boyd and Genevieve Stearns, Iowa City.—p. 594.
Pertussis Antibodies in Pregnant Women: Protective, Agglutinating and Complement Fixing Antibodies Before and After Vaccination. Lucy Mishulow, Lillian Leifer, Catherine Sherwood, Stella L. Schlesinger and Sadie R. Berkey, New York.—p. 608.
Illness History and Physical Growth: I. Correlation in Junior Children Followed from Fall to Spring. Elizabeth J. Martens and H. V. Meredith, Iowa City.—p. 618.
Acute Anterior Poliomyelitis in Kern County, California. Beatrice F. Howitt, San Francisco; W. C. Buss, Bakersfield, Calif., and M. D. Shaffrath, San Francisco.—p. 631.
Peptic Ulcer in Childhood. A. B. Newman, New York.—p. 649.
Icterus Index of Cord Blood: Genesis of Icterus Neonatorum. B. Schick, S. B. Weiner and Miriam Reiner, New York.—p. 655.
Gonadotropins and Linear Growth: Pituitary-Gonadal Mechanism and Its Relation to Linear Growth and Sexual Development. G. B. Dorff, Brooklyn.—p. 661.
Changes in Size and Contour of Thorax During First Postnatal Week. J. L. Goodman, Iowa City.—p. 674.
Osteomyelitis of Long Bones in Newborn. S. Stone, New York.—p. 680.
Ancient Processes in a Scientific Age: Feeding Aspects. C. A. Aldrich, Chicago.—p. 714.

Acidosis with Late Rickets.—To their previous studies of 3 children with late rickets and imbalance of acid-base metabolism, in 1 of whom the rickets was healed through the regular ingestion of sodium bicarbonate, Boyd and Stearns add a fourth patient with late rickets and chronic acidosis whom they have observed intermittently for three years during which time her rickets and osteoporosis healed and remained so under base therapy. Concurrently, most of her metabolic anomalies were controlled and the electrolyte values were restored toward normal levels.

American Journal of Public Health, New York

32:1089-1208 (Oct.) 1942

Epidemiologic Implications of Wartime Population Shifts. K. F. Maxcy, Baltimore.—p. 1089.
Protection of Water and Food Supplies in an Emergency. G. E. Arnold, San Francisco.—p. 1097.
Massachusetts Vision Test: Improved Method for School Vision Testing. Lura Oak, Boston.—p. 1105.
Field Equipment for Food Inspectors. F. A. Korff and E. Kaplan, Baltimore.—p. 1110.
Trends in Public Health Activities Among Negroes in Ninety-Six Southern Counties During the Period 1930-1939: II. Comparison of Certain Health Services Available for Negroes and White Persons. P. B. Cornely, Washington, D. C.—p. 1117.
Evaluation of Health Services in National Emergency. J. W. Mountin, Bethesda, Md.—p. 1125.
*Vaccine Prophylaxis Against Tularemia in Man. L. Foshay, W. H. Hesselbrock, H. J. Wittenberg and A. H. Rodenberg, Cincinnati.—p. 1131.
*Relation of Childhood Infection to Development of Tuberculosis in Early Adult Life. H. L. Israel, Philadelphia, and H. DeLien, Washington, D. C.—p. 1146.
Public Health and Medical Relationships in Industrial Health. O. J. Johnson, Chicago.—p. 1157.
Dissolved Air as Source of Error in Fermentation Tube Results. J. Archambault and M. H. McCrady, Montreal, Canada.—p. 1164.

Vaccine Prophylaxis Against Tularemia.—After many trials on human volunteers with tularemia vaccines made by a variety of chemical procedures, the one that best satisfied Foshay and his co-workers was a vaccine made by oxidation of virulent strains by nitrous acid. Vaccine was administered to 2,145 susceptible individuals exposed to risk of infection. Selection was random and on a volunteer basis. Also during the entire period of preparing the vaccine all laboratory personnel handling virulent cultures and infected animals were vaccinated. The giving of vaccine to recovered individuals was avoided by agglutination tests or cutaneous tests in those with dubious histories. For vaccination three doses of 0.5 cc. each were injected subcutaneously and alternately into the arms on consecutive or alternate days. On annual revaccination applicants were given a trial first injection of 0.25 cc.; the second and third doses varied in accordance with the appearance and degree of reactions. If general and local reactions were definite no more vaccine was given that year, but if there was no general reaction but decided local reaction the subsequent doses were 0.25 cc. each. If neither general nor undue local reaction occurred the subsequent doses were 0.5 cc. each. Data indicate that a useful degree of protection was conferred by annual vaccination. Persons who were not completely protected experienced significant favorable modifications in the course of the disease.

Childhood Infection and Tuberculosis.—Israel and DeLien studied the records of 982 children whose supervision at the Henry Phipps Institute began between 1924 and 1932, with the intention of determining the effect of infection in childhood on tuberculosis in early maturity. Clinically manifest tuberculosis developed in 36 after the age of 14. The disease was fatal in 14. The annual morbidity rate was three to four times as great among the Negro (1.21 per cent) as among the white children of the series. The morbidity among females was considerably higher than among males. The morbidity among the females was largely concentrated in the adolescent years, while among the males it was concentrated in the later years. The mean annual morbidity rate was 0.21 per cent for white males as compared to 0.44 per cent for white females, and 0.54 per cent for Negro males as compared to 1.69 per cent for Negro females. The mean annual morbidity rate was 0.1 per cent in white persons not having household contact after childhood as compared to 2 per cent in white persons having household exposure during adolescence and adult life; the corresponding rates for the Negro group were 0.98 and 3.62 per cent. The morbidity rate in persons who had roentgen evidence of the primary type of tuberculosis was not, in the absence of household contact in adult life, significantly higher than the rate in persons with negative roentgenograms. The rate of 0.33 per cent observed in white persons, relatively few of whom had had preventorium care, was not appreciably higher than the rate calculated from comparable data reported in persons discharged from preventoriums. The study shows that in early adult life exogenous infection is of greater importance than endogenous breakdown of lesions acquired in childhood.

Annals of Surgery, Philadelphia

116:481-640 (Oct.) 1942

Closure of Bronchus Following Total Pneumonectomy: Experimental and Clinical Observations. W. F. Rienhoff Jr., J. Gannon Jr. and I. Sherman, Baltimore.—p. 481.
*Effect of Pneumonectomy on Cardiopulmonary Function in Adult Patients. A. Cournand and F. B. Berry, New York.—p. 532.
Practical Consideration of Open Pneumothorax Under Sodium Evipal, Sodium Pentothal and Ether Anesthesia. C. A. Moyer and J. B. McKittrick, Ann Arbor, Mich.—p. 553.
Transthoracic Resection of Tumors of Esophagus and Stomach. E. D. Churchill and R. H. Sweet, Boston.—p. 566.
*Recent Experiences with Thrombophlebitis of Lower Extremity and Pulmonary Embolism: Value of Venography as Diagnostic Aid. J. Fine, H. A. Frank and A. Starr, Boston.—p. 574.
Control of Hair and Feather Pigmentation as Revealed by Grafting Melanophores in Embryo. B. H. Willier, Baltimore.—p. 598.
Experimental Approach to Problem of Menstrual Disorders. J. C. Burch and Doris Phelps, Nashville, Tenn.—p. 604.
Neurogenic Shock: I. Effects of Prolonged Lowering of Blood Pressure by Continuous Stimulation of Carotid Sinus in Dogs. D. B. Phemister and R. J. Schachter, Chicago.—p. 610.
Stader Reduction Splint for Treating Fractures of Shafts of Long Bones. K. M. Lewis, L. Breidenbach, New York, and O. Stader, Ardmore, Pa.—p. 623.

Effect of Pneumonectomy on Cardiopulmonary Function.—Cournand and Berry present data on various physiologic problems that arose following pneumonectomy on 12 adults from 23 to 64 years of age. The operation was performed on 7

after a diagnosis of carcinoma of the bronchus, on 3 for chronic suppuration of the lung, on 1 because of traumatic fracture of a main bronchus that resulted in stenosis and on 1 for almost complete obstruction of a main bronchus secondary to an endobronchial tuberculosis. The pulmonary volume and subdivisions, the maximal breathing capacity, the ventilation, breathing reserve, respiratory gas exchange and state of the respiratory gases in the arterial blood, under basal conditions, during moderate exercise and during recovery from moderate exercise, and the venous pressure, circulation time and vital capacity before, during and after an infusion of 1,500 cc. of a saline solution in thirty minutes were determined for 10 patients and compared with normal controls. Two of the 10 patients were again studied after a thoracoplasty had been completed and 2, not studied after pneumonectomy, were studied only after thoracoplasty. The chief difference between patients after pneumonectomy and normal subjects was the reduction in their breathing reserve in various states of activity. This reduction caused by a decrease in maximal breathing capacity was greater in the older patients because of the cumulative effect of abnormal hyperventilation. The decrease in maximal breathing capacity was not proportional to the loss of pulmonary volume and was greatly influenced by the state of distention of the remaining lung. The late effects of pneumonectomy on gas exchange in the lungs, respiratory gases in the arterial blood and the cardiocirculatory function were insignificant. In 2 patients aged 53 and 63 distention of the remaining lung due to a mediastinal shift was detrimental to hemorespiratory gas exchange, especially in the older 1, who had pulmonary emphysema. A supplemental thoracoplasty on 4 patients did not further impair the ventilatory function and to some it was of distinct benefit. Overdistention of the remaining lung following pneumonectomy, as far as it impairs the mechanics of the chest bellows and reduces the efficiency of gas exchange, is physiologically undesirable.

Thrombophlebitis and Embolism.—The disadvantages of heparin are that there is no reliable way to identify individuals susceptible to thrombosis and that it will not dissolve a thrombus, so that when the drug is discontinued a propagating clot may still form at the site of the thrombus or a new thrombus may form. There is no way of knowing when it may be safe to discontinue its use. Fine and his associates believe that the procedure of Homans and of other authors in which the femoral vein was divided as a prophylactic measure against embolism in thrombophlebitis of the lower leg has not acquired the vogue it deserves. Results in the authors' first series so treated agreed with those of Homans: embolism did not occur and the phlebitic process in the leg subsided, in some instances at a remarkable rate. Pain decreased or disappeared in a day or two, and edema frequently began to subside more quickly than might be expected. The result was analogous to that obtained by procaine hydrochloride block of the paravertebral sympathetic trunk and was presumed to be due to the breaking of a reflex arc, producing vasospasm and its undesirable sequelae. Their experience with 20 additional patients among whom division of the femoral vein for the prevention of embolism in all cases of thrombophlebitis of the deep veins in the lower leg was practiced has led to the following conclusions: 1. Division of the common femoral vein will cause early resolution of the thrombophlebitic process in the lower leg. 2. The former practice of dividing the femoral vein, by preference below the entrance of the vena profunda, has been abandoned in favor of division above, because of an occasional instance of embolism from the vena profunda. 3. When thrombophlebitis of the lower leg is present, division of the common femoral vein is preferable to heparinization or paravertebral procaine block as a prophylactic measure against embolism. 4. The occasional individual in whom the process does not remain confined to the deep veins in the lower leg must be reclassified as 1 with iliofemoral thrombophlebitis and treated accordingly. 5. If one infarct should occur in such a patient, regardless of the type of management that has been in effect, division of either the common femoral or iliac vein above the site of, or after extraction of, the clot or thrombus should be performed. 6. Venography is an indispensable aid to the correct management of all types of thrombophlebitis of the lower extremity. A filling defect in a venogram does not prove thrombophlebitis unless vasospasm has been ruled out. Until an effective method for achieving this becomes available, the venogram should be interpreted in the light of the concomitant clinical picture. The venogram serves a useful purpose in thrombophlebitis of the lower leg of a patient who complains of pain in the legs before or after becoming ambulatory following operation or prolonged illness but who presents no local signs, in iliofemoral thrombophlebitis, in chronic ulcer of the lower leg and in varicose ulcer.

Archives of Neurology and Psychiatry, Chicago

48:509-688 (Oct.) 1942

Blood Coagulation in Disseminated Sclerosis and Other Diseases of Brain Stem and Cord. B. Simon, Middletown, Conn.—p. 509.
Distribution of Alkaline Phosphatase in Normal and in Neoplastic Tissues of Nervous System: Histochemical Study. H. Landow, E. A. Kabat and W. Newman, New York.—p. 518.
New Tendon Stretch Reflex: Its Significance in Lesions of Pyramidal Tracts. V. E. Gonda, Chicago.—p. 531.
Central Nervous System in Vitamin E Deficient Rats. A. Wolf and A. M. Pappenheimer, New York.—p. 538.
Significance of Insulin Inhibition by Blood of Schizophrenic Patients. M. G. Goldner and H. T. Ricketts, Chicago.—p. 552.
Pyramidal Tract: Study of Retrograde Degeneration in Monkey. A. M. Lassek, Charleston, S. C.—p. 561.
Intelligence in Cerebral Deficit States and Schizophrenia Measured by Kohs Block Test. T. Lidz, J. R. Gay and C. Tietze, Baltimore.—p. 568.
Congenital Atresia of Foramens of Luschka and Magendie. J. K. Taggart Jr. and A. E. Walker, Chicago.—p. 583.
Boeck's Disease (Sarcoid) of Central Nervous System: Report of Case, with Complete Clinical and Pathologic Study. T. C. Erickson, Madison, Wis.; G. Odom and K. Stern, Montreal, Canada.—p. 613.
Vibratory Sensibility: Quantitative Study of Its Thresholds in Nervous Disorders. J. C. Fox Jr. and W. W. Klemperer, New Haven, Conn.—p. 622.

Archives of Otolaryngology, Chicago

36:455-618 (Oct.) 1942

*New Bone Growth Due to Cold Water in Ears. E. P. Fowler Jr., New York, and P. M. Osmun, Houston, Texas.—p. 455.
Ludwig's Angina. C. H. McCaskey, Indianapolis.—p. 467.
Bone Repair Following Defects Made in Skull of Cats by Means of Different Instruments. J. Lempert, New York; P. E. Meltzer and B. Spector, Boston.—p. 473.
Laryngotracheobronchitis in Children: Classification and Differential Diagnosis. T. R. Gittins, Sioux City, Iowa.—p. 491.
Osteoma of External Auditory Canal. J. G. Druss and J. L. Maybaum, New York.—p. 499.
Orbitoethmoidal Osteoma with Infected Intracranial Mucocele: Cerebral Abscess of Unusual Origin. W. B. Hamby, Buffalo.—p. 510.
Infections with Anaerobic Streptococci, with Special Reference to Cranial Osteomyelitis. T. C. Galloway, Evanston, Ill.—p. 514.
Correlation of Hearing Acuity for Speech with Discrete Frequency Audiograms: Method of Determination. W. Hughson and Eva Thompson, Abington, Pa.—p. 526.
Masking of Pathologic Status in Otitis Media by Chemotherapy. A. A. Cirillo, Jamaica, N. Y.—p. 541.
Reflex Effects Produced by Abnormal Movement of Lower Jaw. J. B. Costen, St. Louis.—p. 548.
Tumors of Nose and Throat. G. B. New and J. B. Erich, Rochester, Minn.—p. 566.

Bone Growth from Water in Ears.—Van Gilse observed exostosis in the external auditory canal of cold water swimmers. Fowler and Osmun encountered, in three years, 25 patients with hyperostosis and 9 with discrete exostosis of the external auditory canal. Changes produced in auditory canals of guinea pigs by cold water were striking not in the external auditory meatus but in the middle ear. There was diffuse production of new bone in the submucosa of the bulla of the middle ear on the experimental side. The new bone formation was more or less proportional to the number of times the cold water was used as a stimulus. There were no changes in the labyrinthine capsule except for slight growth of new bone on the most exposed portion of the promontory. Microscopic evidence was not sufficient to explain the formation of new bone on the basis of infection. In the external canal of the experimental ears, slight fibrosis and hyalinization of the soft tissue and occasionally a small amount of new bone was present. This alteration was never sufficiently striking, as compared with the control side, to be of certain experimental origin. The observation of van Gilse that cold water swimming can often cause discrete exostosis or hyperostosis of the external canal is confirmed.

Journal of Clin. Endocrinology, Springfield, Ill.

2:577-614 (Oct.) 1942

Clinical Reviews in Andrologic Endocrinology: I. Physiology, Functional Pathology and Diagnosis. R. L. Pullen, J. A. Wilson, E. C. Hamblen and W. K. Cuyler, Durham, N. C.—p. 577.
Clinical Determination of Pregnandiol Excretion. H. Wooster, Madison, Wis.—p. 588.
Disposal of Glucose at High and Normal Blood Sugar Levels Under Action of Insulin. P. O. Greeley, Helen E. Martin and Lois F. Hallman, Los Angeles.—p. 590.
*Insulin Allergy: Report of Eight Cases with Generalized Symptoms. M. G. Goldner and H. T. Ricketts, Chicago.—p. 595.
Present Status of Use of Male Sex Hormones and Chorionic Gonadotropins as Growth Stimulating Factors. Rita S. Finkler, N. J. Furst and G. M. Cohn, Newark, N. J.—p. 603.

Insulin Allergy.—Goldner and Ricketts use the term "allergic" in referring to symptoms due to the antigenic property of insulin as a protein substance, and sensitivity and insensitivity in referring to the response of the body to the specific metabolic function of insulin as a hormone. About 20 per cent of persons within a week to ten days of beginning treatment with insulin have swelling and erythema at the site of injection which persist for thirty minutes to several hours. Itching and induration may be present. Usually these reactions will not interfere with the action of insulin and will disappear without special care after ten days or two weeks. Sometimes changing the brand of insulin may be helpful. In a few patients the reactions increase in severity, extend in size and spread over the body, causing generalized urticaria with involvement of the mucous membranes, severe pruritus, articular pain, headaches, elevated temperature and circulatory gastrointestinal symptoms. These reactions do not subside spontaneously but require desensitization or discontinuance of treatment. The observation on generalized insulin allergy in 8 patients encountered by the authors in the metabolism clinic of the Billings Hospital from 1937 to 1941, and the 15 from the literature, indicates that this condition occurs predominantly in middle aged or older patients with moderately severe diabetes. Interrupted treatment with insulin predisposes to allergy. Cutaneous tests are advisable for all patients of whom treatment is resumed and for those with clinical symptoms suggestive of insulin allergy.

New England Journal of Medicine, Boston

227:427-464 (Sept. 17) 1942

Physician's Status in Child Guidance Work. P. Solomon, Boston.—p. 427.
Observations Concerning Pulmonary Fibrosis in Raynaud's Disease: Report of Two Additional Cases. H. Linenthal, Boston.—p. 433.
Tuberculosis of Foot and Ankle in Adults and Children. J. D. Wassersug, Middleboro, Mass.—p. 436.
Alcohol and Cerebral Vasodilatation. J. Loman and A. Myerson, Boston.—p. 439.
Treatment of Rheumatoid Arthritis. C. L. Short and W. Bauer, Boston.—p. 442.

227:465-498 (Sept. 24) 1942

*Sulfonamide Therapy in Gonococcic Infection in Women and Children: Sulfanilamide, Sulfapyridine, Sulfathiazole and Sulfadiazine. F. L. Adair and Lucile R. Hac, Chicago.—p. 465.
Significance of Carotid Sinus Reflex in Biliary Tract Disease. G. L. Engel and F. L. Engel, New York.—p. 470.
Quinine Methochloride Treatment of Spastic Children: Preliminary Report. E. Press, East Providence, R. I.—p. 475.
Rare Type of Acute Thrombocytopenic Purpura: Widespread Formation of Platelet Thrombi in Capillaries. M. D. Altschule, Boston.—p. 477.
Surgical Care and Operative Technic. J. D. Stewart, Buffalo.—p. 480.

Sulfonamide Therapy in Gonococcic Infection.—Adair and Hac treated 453 ambulatory women and 80 children for gonorrhea with one of the sulfonamide derivatives. Cures were obtained in 52, 49, 65 and 75 per cent of the patients treated respectively with sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine. Patients were designated as cured when tests remained negative through two consecutive menstrual periods followed by negative provocative tests. Failures (16, 8, 5 and 3 per cent respectively for the four drugs) occurred in patients from whom evidence of reinfection could not be elicited. Most of them had cultures that remained consistently positive throughout treatment. All the delinquent cases (8, 13, 3 and 7 per cent) were negative for more than a month and were probably cured, but as further observation was not possible they are not considered as cured. Reinfections (34, 30, 27 and 15 per cent) were considered probable in patients who either had spermatozoa in their smears or admitted sexual contact. Women responded rapidly to sulfonamide therapy and became noncontagious much earlier than with local treatment. Of those cured with sulfathiazole, 97 per cent had negative smears and cultures within four days of treatment, and of the ones treated with sulfadiazine 98 per cent responded within four days. Secondary complications were rare when sulfonamides were administered early. None of the patients discharged as cured required surgical treatment for complications. There was only one drug fast strain of gonococci among the 453 women. Sulfathiazole appears to be the drug of choice for vulvovaginitis in children. Sulfanilamide is contraindicated because it tends to produce drug fast strains.

Northwest Medicine, Seattle

41:331-366 (Oct.) 1942

What Is Wrong with the American Diet? A. J. Carlson, Chicago.—p. 334.
Vitamins in General Practice: Treatment of Certain Types of Heart Disease. O. J. Morehead, Ritzville, Wash.—p. 337.
Intestinal Obstruction. H. B. Stone, Baltimore.—p. 340.
War Wounds at the Surgical Station. R. deR. Barondes, Los Angeles.—p. 343.
*Gunshot Wounds of Liver. C. W. Countryman, Spokane, Wash.—p. 346.

Gunshot Wounds of Liver.—Countryman advocates the following principles in treating gunshot wounds of the liver: rapid and immediate surgery, control of hemorrhage, muscle transplant tamponade of the liver injury, search for additional visceral injuries, prevention of slough and infection of the entering wound, treatment of shock, rest with adequate morphine therapy, sulfonamides, tetanus toxoid and postoperative treatment which includes repeated urinalysis, transfusions, determination of the icterus index and leukocyte counts and drainage to control the infection which is always present. Secondary hemorrhage and sepsis are the most frequent causes of death. Through rapid efficient handling of this serious abdominal emergency and the application of an easily obtained transplant which would obviate gauze packing and its removal, a small percentage of lives may be saved.

Ohio State Medical Journal, Columbus

38:893-988 (Oct.) 1942

*Combined Artificial Fever Chemotherapy in Treatment of Neurosyphilis: Summary of Ten Years' Experience. H. W. Kendell, W. M. Simpson and D. L. Rose, Dayton.—p. 909.
Tumors of Mediastinum. S. O. Freedlander, Cleveland.—p. 919.
Management of Acute Infections of Hand. V. E. Siler, Cincinnati.—p. 922.
*Mechanism for Production of Kidney Complications in Sulfonamide Therapy. R. W. Monto, Detroit, Mich.—p. 925.
*Sulfonamide Anuria. W. A. Keitzer and J. A. Campbell, Akron.—p. 929.
Pulmonic Interstitial Emphysema and Anterior Mediastinal Emphysema. G. X. Schwemlein, Cincinnati.—p. 932.
Acute Inversion of Puerperal Uterus. R. Patton and C. W. Pavey, Columbus.—p. 935.
The Trace Mineral Elements in Nutrition. J. Forman, Columbus.—p. 937.

Artificial Fever and Chemotherapy in Treatment of Neurosyphilis.—Since 1931 Kendell and his associates have subjected 1,376 patients to artificial fever therapy. Of the 271 patients treated for neurosyphilis the records of 64 were excluded from consideration because of incomplete observation. Of the remaining 207, 52 per cent had remissions and an additional 28 per cent were improved by the treatment. The concurrent use of chemotherapy with artificial fever therapy increases the therapeutic effectiveness of both agencies. Recent developments have demonstrated that equally favorable clinical and serologic results may be obtained with fewer total hours of artificial fever therapy applied during shorter individual sessions at more frequent intervals. This permits the treatment of more patients at less cost.

Renal Complications from Sulfonamide Therapy.—Conditions which favor occurrence of renal disease with sulfonamide therapy, according to Monto, are previous renal damage, toxicity of the disease, idiosyncrasy to the drug, the quantity of the drug given in a unit of time, the general condition of the patient and the sulfonamide drug used. The sulfonamides are toxic materials and may act on the kidneys in a manner similar to other renal irritants producing toxic nephritis. A second intrarenal lesion is found in those patients in whom a preexisting nephritis was present and in whom reabsorption of the drug in the convoluted tubules is faulty. This results in an increased

concentration and deposition of the drug in a crystalline form in the tubules. As for extrarenal lesions, anuria and anemia have been reported to result from intravascular hemolysis as produced by sulfanilamide and by plugging of both ureters with calculi of the drug. Several facts cast doubt on the principle that most of the anurias are caused by precipitation of the acetylated drug in the tubules. If anuria were so produced the quantitative analysis of renal tissue would show a much higher renal concentration of the acetylated form of the drug. Anuria due to complete occlusion (plugging) of collecting tubules, from multiple myeloma and from crush syndrome has been previously reported. Treatment of anuria following sulfonamide therapy is chiefly prophylactic and consists of fluid intake, daily determination of the blood level of the drug, daily urinalysis in search of albumin and blood cells and the discontinuance of the drug at the first sign of renal failure. Immediate catheterization of both ureters is indicated when anuria occurs and if the patient has signs and symptoms of renal colic with diminution of renal output. In the event of mechanical blocking the renal pelvis should be irrigated with warm saline solution to dislodge the calculus. If the anuria is not mechanical the usual therapeutic measures are indicated. Stripping the renal capsule has resulted in the resumption of renal function in a few cases.

Sulfonamide Anuria.—Keitzer and Campbell report their ninth and tenth cases of sulfonamide anuria; both followed sulfapyridine therapy. Both patients were cured by ureteral lavage and aspiration at frequent intervals. Concretions reformed in the urinary tract of 1 patient when the catheters were withdrawn prematurely. If anuria reappears, a repeated cystoscopy is indicated. Forcing of fluids expedites recovery. No permanent renal damage was sustained. The authors have had no deaths from sulfonamide anuria. They believe that concretions form in the urinary tract on a mechanical basis. Once in the ureters they are difficult to dislodge. A small urinary output does not effectively cleanse the lower ends of the ureters of crystals. The concretions then form in thrombotic-like fashion.

Psychiatric Quarterly, Utica, N. Y.

16:633-854 (Oct.) 1942

Two Factors in Prognosis of Alcoholism. J. M. Nagle, San Francisco. —p. 633.

On Fear of Being Buried Alive. S. Feldman, Rochester, N. Y.—p. 641.

Contrasting Schizophrenic Patterns in Graphic Rorschach. J. R. Grassi, Newtown, Conn.—p. 646.

Ward Therapy: New Method of Group Psychotherapy. N. Blackman, Clarinda, Iowa.—p. 660.

*Prognosis of Carbon Monoxide Poisoning in Fifteen Patients Previously Mentally Ill. R. J. Van Amberg, White Plains, N. Y.—p. 668.

Massive Structure of Delinquency. A. N. Foxe, New York.—p. 681.

Passing the Meridian of Life. G. M. Davidson, Ward's Island, N. Y. —p. 692.

Rorschach Method and Postconcussion Syndrome. J. A. Brussel, J. R. Grassi and A. A. Melniker, Fort Dix, N. J.—p. 707.

Review of a Year of Group Psychotherapy. J. R. Jacobson and Katharine W. Wright, Elgin, Ill.—p. 744.

Physiologic Factors in Treatment of Mental Disorders. T. V. Moore, Washington, D. C.—p. 765.

Adlerian Approach to Case of Idiopathic Epilepsy. R. Rosenberg, Central Islip, N. Y.—p. 780.

Prognosis of Carbon Monoxide Poisoning.—The records of 15 mentally disordered patients who had attempted suicide by illuminating gas or motor exhaust gas were studied by Van Amberg to determine the factors that might indicate or influence the course of the toxic exchanges. One patient survived three serious exposures to illuminating gas; all the others survived one exposure. Illuminating gas was chosen by 11 and motor exhaust gas by 4. Sensorium or neurologic changes were not experienced by 4 patients who were sufficiently exposed to cause acute symptoms but not unconsciousness, nor were changes suffered by the 4 who were unconscious up to thirty minutes. Two patients who were unconscious about one hour had transient neurologic changes; 1 enjoyed an intact sensorium but the other encountered the complication of cerebral arteriosclerosis. The 5 patients who were unconscious from three hours to ten days showed extreme variability in the power of recovery. Apparently a patient poisoned by carbon monoxide is not likely to have serious sequelae if he regains consciousness within one hour after being removed from the toxic atmosphere. There was no important clinical difference between the toxicity of motor exhaust gas and that of illuminating gas.

Radiology, Syracuse, N. Y.

39:253-382 (Sept.) 1942

Normal Stomach and Small Intestines in Infant. J. S. Bouslog, Denver. —p. 253.

Colon in Healthy Newborn Infant. S. G. Henderson and W. W. Briant Jr., Pittsburgh.—p. 261.

Clinical Aspects of Gastrointestinal Disease in Childhood. W. C. Deamer and C. S. Capp, San Francisco.—p. 273.

*Cancer in Childhood. M. Ritvo, J. D. Houghton and E. J. McDonald, Boston.—p. 278.

Value of Roentgen Rays in Diagnosis of Endocrine Diseases. P. J. Connor and F. J. Maier, Denver.—p. 283.

Roentgenographic Appearance of Bones in Cushing's Syndrome. M. L. Sussman and B. Copleman, New York.—p. 288.

*Results of Irradiation Treatment of Cancer of Lip: Analysis of 636 Cases from 1926-1936. B. F. Schreiner and C. J. Christy, Buffalo. —p. 293.

Panel Discussion on Leukemias and Lymphoblastomas. R. R. Newell, E. H. Falconer, J. H. Lawrence, H. P. Hill, D. A. Wood and H. Wyckoff, San Francisco.—p. 298.

Technic for Chest X-Ray Examinations of Large Groups: I. Use of Standard Size Films. W. Bailey, Los Angeles.—p. 306.

Id.: II. Use of Miniature Films. W. Bailey, Los Angeles.—p. 310.

Study of Limiting Diaphragm Method of Collimation. S. M. Silverstone and B. S. Wolf, New York.—p. 314.

Roentgenologic Aspect of Pseudomyxoma Peritonaei. D. G. Pugh, Rochester, Minn.—p. 320.

Cardioangiography. H. K. Taylor, New York, and I. Shulman, Washington, D. C.—p. 323.

Cancer in Childhood.—Ritvo and his associates point out that, according to the census, 153,846 persons died of cancer in the United States during 1939, and 1,103, or 0.7 per cent, of these were less than 15 years of age. The vital statistics of Massachusetts for 1939 further show that the death rate for cancer in childhood was greater than for pertussis, pulmonary tuberculosis, measles, diabetes, cerebrospinal meningitis, syphilis, scarlet fever or typhoid; the only diseases which had higher death rates were "influenza," diseases of the nervous system, appendicitis, diarrhea, the enteric diseases and pneumonia. During the last twenty-five years the number of deaths from cancer in children has increased, while for many diseases common in infancy and childhood there has been a progressive decrease. At the Boston City Hospital from 1915 to 1939 inclusive, 72 children died of malignant neoplasms. Twenty-three were intracranial neoplasms, and tumors of the kidney comprised the second largest group, 13. The most common tumors were glioma (medulloblastoma, astrocytoma and mixed gliomas), Wilms's tumor, osteogenic sarcoma, Ewing's sarcoma and miscellaneous soft tissue sarcomas. There were 3 examples of carcinoma of the adult type. Among the earliest instances of cancer were a Wilms tumor at 1 year, a medulloblastoma at 1 and 2 years and a fibrosarcoma at 2 years. The only congenital tumor in the series was a malignant teratoma of the orbital region.

Irradiation of Cancer of Lip.—From January 1926 to January 1936, 636 cases of cancer of the lip were irradiated at the State Institute for the Study of Malignant Diseases. According to Schreiner and Christy, cancer of the lip occurred thirty-eight times more frequently in men than in women, and about twenty-nine times as often on the lower as on the upper lip. There were 619 men and 17 women. The upper lip of 22 was involved, 2 of whom were women. The youngest patient was 28 and the oldest 92. The climatic conditions to which farmers, postmen, painters and the like are subjected was an etiologic factor; 201 of the 636 cases fell into this category. The use of tobacco was common; 546 of the men and 7 of the women used it. The oral hygiene of 258 was considered to be bad. In 389 there was a history of cracked or chapped lips or chronic fissure; 197 cases presented definite histories or signs of keratosis. Of 334 patients with primary cancer and no demonstrable metastasis or enlarged lymph nodes 232 remained well five years or longer, 69 died from intercurrent disease with the local lesion healed, 18 were lost from observation with the local lesion healed and 15 died of uncontrollable metastasis. The absolute cure rate for the group is 69.5 per cent. Of 192 patients with primary cancer and palpable, movable lymph nodes (and probable metastasis in some) 131 remained well five years or longer, 19 died of intercurrent disease with the local lesion healed, 19 were lost from observation with the local lesion healed and 23 died from the disease. The absolute cure rate for the group is 68.2 per cent. Of 110 patients with primary

cancer and definite metastasis, 12 were well five years or longer, 6 were lost from observation with unascertained results, 1 died from intercurrent disease with the primary lesion healed and the metastatic nodes sclerosed and 91 died from metastasis. The absolute cure rate for this group is 10.9 per cent. The absolute cure rate for the total series is 58.9 per cent. If the patients who died of intercurrent disease with a lesion healed and those who were lost from observation with the lesion healed less than five years are eliminated, the cure rate is 74.4 per cent.

Southern Medical Journal, Birmingham, Ala.

35:869-958 (Oct.) 1942

*Geographic Pathology of St. Louis Encephalitis. A. E. Casey, Birmingham, Ala.—p. 869.
Regional Ileitis. A. K. Wilson, R. B. Grinnan and H. G. Ashburn, Norfolk, Va.—p. 881.
Corneal Vascularization in Ariboflavinosis. W. Cochran, N. M. DeVaughn and L. Allen, Augusta, Ga.—p. 888.
Treatment of Granuloma Inguinale. H. M. Robinson and H. M. Robinson Jr., with surgical assistance of H. S. Shelley and H. B. Mays, Baltimore.—p. 889.
Technic of Pyelography. H. M. Young, Columbia, Mo.—p. 895.
Individualized Anesthesia. H. M. Ausherman, Chattanooga, Tenn.—p. 903.
Bacterial Allergy: Otolaryngologic Aspects. W. W. Eagle, Durham, N. C.—p. 908.
Occupational, Seasonal Hay Fever and Asthma Due to Narcissus Bulbs. V. J. Derbes, New Orleans.—p. 912.
*Differentiation of Bronchial Asthma from Sighing Dyspnea and Cardiac Asthma. W. H. Browning, Shreveport, La.—p. 914.
Treatment of Lichen Planus. A. H. Conrad, St. Louis.—p. 918.
*Mineral Oil and Saline Laxatives: Relationship to Anorectal Infections and Their Treatment. G. H. Thiele, Kansas City, Mo.—p. 920.
Dynamic Approach to Psychopathic Personality. L. F. Woolley, Towson, Md.—p. 926.
Mental Hygiene Program in State Health Department. A. M. Gaulocher, Montgomery, Ala.—p. 934.
Medical Phases of Industrial Hygiene as Related to Work of Health Departments. J. G. Townsend, Bethesda, Md.—p. 939.
General Practitioners and Pediatricians: Rivals or Co-Workers. J. P. Price, Florence, S. C.—p. 944.

Geographic Pathology of St. Louis Encephalitis.—Casey describes the methodology of the original study in the St. Louis area of the epidemic of St. Louis encephalitis in 1933 and 1937 and offers evidence that the disease was not spread along the traveled highways, boulevards, interstate railways or navigable streams but along small streams which carried sewage and in areas characterized by weeds, garbage and tin can dumps. The encephalitis was significantly scarce in both epidemics in areas not characterized by weeds, open sewage and ponds. Using an adequate control series and biometric methods, no foci were found along the most traveled highways in St. Louis County, along the principal boulevards in St. Louis or along the interstate railroads, and also there was no relation of the disease to congested housing. The disease occurred in the same districts in 1933 and in 1937. Its distribution was different from that of measles. The possibility of a mosquito vector was considered. During both epidemics it was a hot, dry year, when evaporation was rapid and sewage concentration was unusual. Something existed along these streams in the weed and tin can areas which started the disease in the same places in two different epidemics and which remained there throughout both epidemics. Such a distribution is for Culex mosquitoes and not, so far as is known, for ticks.

Bronchial Asthma, Sighing Dyspnea and Cardiac Asthma.—The same prominent signs and symptoms may be produced by conditions other than bronchial asthma. Sighing dyspnea and cardiac asthma, the one without wheezing, the other with wheezing, Browning points out, are sometimes confused with bronchial asthma. The syndrome of sighing dyspnea consists of deep sighing respirations which are greatly increased in depth without much alteration in the respiratory rate. The shoulders are elevated with each inspiration and the accessory respiratory muscles act as in an asthmatic attack. The face shows anxiety and distress, and the patient often puts one or both hands to the thorax. It is not uncommon for the patient to run outdoors to get sufficient air. If the attack is long and severe, tetany may occur from hyperventilation. A correct history is the only means of differentiating such an attack from bronchial asthma. The patient should be questioned in detail concerning wheezing, and during the course of taking the history the patient will often take a deep sighing inspiration. This should give one a clue, but if it does not the stereotyped phrases "I just can't get a deep breath," "I just breathe below this," "I just can't get a satisfying breath," "something prevents air from going to the bottom of my lungs" or "something seems to press on my chest" that the patient uses should suggest the diagnosis. After a patient has given such a lead it is usually a simple matter to determine definitely that he does not have bronchial asthma. Sighing dyspnea is a functional disorder; it may coexist with organic disease, but its underlying cause is always a nervous disorder requiring treatment. Cardiac asthma results from left ventricular failure, but not all persons with left ventricular failure have cardiac asthma. Swineford has reached the conclusion that the cardiac failure has thrown the patient out of allergic balance. This affords an explanation of why some patients with left ventricular failure have asthmatic symptoms whereas others do not. Even though it is assumed that cardiac asthma is nothing more than heart failure in an allergic individual it is still necessary to know that cardiac failure is the underlying cause. Epinephrine is almost a specific for bronchial asthma but may be detrimental to the patient with cardiac asthma. Morphine is almost a specific for cardiac asthma but may be harmful in bronchial asthma. When ordinary means of differential diagnosis fail, circulation time tests are invaluable. The only two tests essential are relatively simple; they are the "arm to lung time" and the "arm to tongue time."

Liquid Petrolatum and Saline Laxatives.—Thiele presents evidence that liquid petrolatum and saline laxatives bear a direct relationship to the incidence of acute anorectal infections. When liquid petrolatum or saline laxatives are taken, the passage of the resultant stool is impossible without an oily or watery suspension of bacteria existing under pressure at the mouths of the anal crypts. The suspension is therefore forced into the anal crypts and possibly also into their tributary ducts. Whether or not an acute cryptitis ensues depends on whether the crypts have been previously traumatized, whether or not upper respiratory or enteral infection coexists, the bacteria of which will contaminate the stool, and whether the anal membrane and crypts were irritated by chemical substances contained in the laxative stool, giving the intestinal enzymes insufficient time to accomplish normal intestinal digestion. Once the anal crypt is infected, the infection spreads distally, the anal membrane loses its normal elasticity, fissure results and its subsequent ulceration produces an anal ulcer. Of 160 patients with anal ulcer, the so-called ulcerated anal fissure, for whom accurate records were had, 67 had taken liquid petrolatum when they consulted the author. Fifty-eight of these had taken the liquid petrolatum either habitually or in large doses for acute dyschesia, immediately preceding the onset of anal symptoms. Only 9 of the 67 gave a history of having begun its use after the onset of acute symptoms of anal fissure or ulcer. Thirty-three additional patients had taken other laxatives, either habitually or immediately preceding the onset of anal symptoms. The question of whether liquid petrolatum or saline laxatives bear any causal relationship to anal infections was studied in a controlled group of obstetric patients who were instructed to use one of the gum laxatives (instead of the liquid petrolatum or saline ones) without cascara, have a smooth diet in the latter half of pregnancy and drink from twelve to fifteen glasses of water daily unless otherwise contraindicated. Since adopting these simple measures, only 6 of 350 mothers delivered had any rectal complaint or any anorectal disease. Furthermore, the proctitis of these 6 was attributed to improper mixing of the ether and liquid petrolatum for rectal anesthesia. In contrast to this experience, 5 per cent of 1,275 obstetric patients at the obstetric clinic at the University of Kansas School of Medicine, where 1 tablespoon twice a day of plain liquid petrolatum is prescribed routinely for all patients who need a laxative, had anorectal disease. The study raises the question as to whether abnormal bleeding from hemorrhoids or other anorectal lesions may be due to the habitual use of liquid petrolatum by some patients. That liquid petrolatum delays the healing of anorectal wounds is well known. Its administration reduces the blood prothrombin level and may account for some abnormal hemorrhage.

Surgery, Gynecology and Obstetrics, Chicago

75:401-546 (Oct.) 1942

Traumatic Shock: Consideration of Several Types of Injuries. A. Blalock and G. W. Duncan, Baltimore.—p. 401.
*Plasma Therapy in Severe Burns. H. N. Harkins, C. R. Lam and H. Romence, Detroit.—p. 410.
Blood Vessels of Female Pelvis in Relation to Gynecologic Surgery. A. H. Curtis, B. J. Anson, F. L. Ashley and T. Jones, Chicago. —p. 421.
*Residual Lesions of Ulcerative Gastritis: Possible Relationship to Development of Carcinoma of Stomach. E. S. Judd Jr., Rochester, Minn.—p. 424.
Shoulder Joint: Observation on Anatomy and Physiology with Analysis of Reconstructive Operation Following Extensive Injury. L. Jones, Kansas City, Mo.—p. 433.
Surgical Exposure of Gallbladder and Bile Ducts. F. H. Lahey, Boston. —p. 445.
Surgical Repair of Recent Lid Lacerations: Intramarginal Splinting Suture. H. Minsky, New York.—p. 449.
*Surgical Treatment of Bilateral Bronchiectasis. B. Blades and E. A. Graham, St. Louis.—p. 457.
End Results in 100 Consecutive Cases of Brain Abscess. F. C. Grant, Philadelphia.—p. 465.
Mechanical Skeletal Fixation in War Surgery: Report of Sixty-One Cases. C. Bradford, Boston, and P. D. Wilson, New York.—p. 468.
Mechanism of Labor for Transverse Positions of Vertex. K. B. Steele and C. T. Javert, New York.—p. 477.
Aseptic Gastrointestinal Anastomosis: One Clamp Method of Universal Application. W. W. Babcock, Philadelphia.—p. 485.
Surgical Treatment of Carcinoma of Pharynx and Upper Esophagus. H. Wookey, Toronto, Canada.—p. 499.
Laminagraph as Aid in Treatment of Chronic Osteomyelitis. A. D. Smith and L. E. Miller Jr. New York.—p. 507.
Roentgenologic Study of Postoperative Abdomen. J. Levitin and L. M. Trauner, San Francisco.—p. 510.
Vitamin E in Prophylaxis of Abruptio Placentae. E. Shute, London, Ont., Canada.—p. 515.

Plasma Therapy in Severe Burns.—The general treatment of burns attempts to bring the patient past four serious chronologic stages of a burn: primary shock, secondary shock, toxemia and infection. The progressive development of these stages requires that treatment be instituted rapidly, carried out continuously and followed meticulously for as long a time as necessary. Harkins and his associates state that plasma administration is the best form of treatment for primary and secondary shock due to hemoconcentration from loss of plasma into the tissues. Administration of plasma should be quantitatively adjusted to fit the patient. For calculating the necessary dose of plasma, when no laboratory facilities are available, the first aid formula should be utilized, that is 50 cc. of plasma for each per cent of the body surface (as calculated by the Berkow method) involved by a deep (blistering) burn. There are three methods of calculating hemoconcentration. The formulas of Black and of Elkinton are accurate, but the authors believe that the Harkins formula is therapeutically just as reliable and is much simpler. This method is as follows: The amount of plasma needed can be roughly calculated for an average size adult as being 100 cc. of plasma for every point the hematocrit exceeds the normal of 45 as long as the plasma proteins are above 6 Gm. per hundred cubic centimeters. When the plasma proteins are below this level an additional 25 per cent of the calculated amount of plasma should be added for every gram the protein is below 6 Gm. Preventive measures against toxemia and sepsis should be carried out along with shock therapy. Toxemia is apt to occur during the second to the fourth day after a burn. Jaundice, increase in the icteric index, decrease in the urinary output, stupor and a demonstrable decrease in hepatic function are prodromal signs. Adequate dextrose and sufficient sodium chloride to maintain equilibrium are indicated. The reasonable use of these crystalloid solutions and adrenal cortex extract to prevent burn toxemia conforms with the control of burn shock. Sepsis is largely preventable by careful local therapy and adequate chemotherapy.

Residual Lesions of Ulcerative Gastritis.—Judd evaluates the significance of changes in the gastric mucosa which take place over many years as related to the development of gastric carcinoma. The material examined consisted of 200 carcinomas of the stomach removed at operation and/or necropsy at the Mayo Clinic between 1926 and 1938. For control 78 average stomachs, which were obtained at routine postmortem examination of patients without gastric carcinoma, were examined. For convenience the residual lesions were placed in seven separate columns: accumulation of lymphocytes, irregularity of the muscularis mucosae, thickening of the muscularis mucosae, fibrosis of the muscularis mucosae, atrophy of the chief and parietal cells, hyperplasia of the mucous cells and disorganization of the mucosal glandular elements. Of the 200 carcinomas not 1 could be placed entirely outside the columns of classification. The control group contained 5 completely free instances. When the final tabulations of the grades of change were examined, certain of the "residual lesions" could not in themselves be regarded as of prime significance in the development of the carcinoma. The most common change in all specimens, whether cancer or control, was the accumulation of lymphocytes in the mucosa, either in so-called follicles or in diffusely scattered array. The evidence obtained by tabulation of the grade of change in the five residual lesions considered of secondary importance in the pathogenesis of carcinoma was found to be invaluable in the study of the chronicity of the disease. This left for serious primary consideration only two of the residual lesions: atrophy of the chief and parietal cells and hyperplasia of the mucous cells. Atrophy of the specialized epithelial cells was a frequent and consistent observation in the cancer group; in sections made directly through the tumor, 98.5 per cent, and in those cut 10 cm. from the edge of the cancer, 91.5 per cent. Hyperplasia of the mucous cells in these two groups was only slightly less frequent, 89.5 and 83.5 per cent respectively. In the control group atrophy was present in 57.6 per cent and hyperplasia in 37 per cent. The consistently lower incidence and decidedly less prominent degree of hyperplasia in the control group lend support to the conclusion that hyperplasia (regenerative activity) is a highly important factor in the pathogenesis of gastric carcinoma. Gastric analysis was recorded for 124 of the 200 patients with carcinoma, and 96 of these had no free acid. The neoplasm of 20 of the 200 was suspected clinically of originating as a gastric ulcer. If these "former ulcer" cases could be disregarded, it would seem that an excellent clinical indicator of the ability of the stomach itself to ward off carcinoma would be the presence of a normal amount of free hydrochloric acid. Hurst expressed much in a few words when he said that carcinoma does not develop in a healthy stomach.

Surgical Treatment of Bilateral Bronchiectasis.—Blades and Graham performed total pneumonectomy for bronchiectasis on 4 children less than 8 years of age. All recovered. The exact precedents for bilateral extirpation of pulmonary tissue are not yet established but the principal considerations are the age and general condition of the patient, the amount of tissue involved, the degree of involvement and the severity of symptoms. It is the authors' opinion that an operation is rarely justified for patients past middle age with bilateral disease. Cardiovascular disease and other serious conditions preclude lobectomy. The amount of tissue that may be extirpated safely is influenced by a consideration of vital capacity, age and other individual factors. Their experience with 16 other cases of bilateral bronchiectasis, in 4 of which all the tissue but the two upper lobes was removed, has convinced them that in young subjects two pulmonary lobes furnish adequate respiratory exchange for ordinary physical activities. The decision for bilateral lobectomy will therefore depend somewhat on the amount of sputum raised and the inconvenience and disability, that is, the severity of symptoms, that the foul sputum causes the patient. For older patients with bilateral disease and mild symptoms, postural drainage, supplemented in some by bronchoscopic aspiration, should be given a fair trial before lobectomy is undertaken. There were four deaths following the twenty lobectomies for bilateral bronchiectasis. Two deaths had no connection (one from tuberculous pneumonia and one from staphylococcic septicemia) with the bilateral distribution of the disease. The chief danger from bilateral lobectomy is suffocation during the operation or from early opening of the bronchus. The upright position for lobectomy minimizes the danger of suffocation, relieves the necessity of rapid operating and allows time for an adequate closure of the bronchus. The oldest patient in the group operated on was 44; lobectomy was performed because, in addition to raising foul sputum, he was completely incapacitated by an intractable cough caused by a partial stenosis of the right lower lobe bronchus. From the patient's standpoint the result of unilateral lobectomy was entirely satisfactory.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Children's Diseases, London

39:65-96 (July-Sept.) 1942

Nephrotic Dwarfism with Glycosuria and Rickets of Low Phosphorus Type. R. Aidin and E. Nobel.—p. 65.
Medical or Surgical Treatment of Pyloric Stenosis. S. Engel.—p. 72.

British Journal of Dermatology and Syphilis, London

54:223-254 (Aug.-Sept.) 1942

Dermatologic Experiences with British Expeditionary Force, France (1939-1940). J. T. Ingram.—p. 223.
Late Cutaneous Recurrence of South American Leishmaniasis After Treatment with Antimony. J. F. Smith.—p. 231.
General X-Ray Baths in Generalized Dermatoses. J. Sommerville.—p. 234.

Journal of Hygiene, London

42:339-450 (July) 1942

Evaluation of Bactericides. E. R. Withell.—p. 339.
Chemical and Physical Investigation of Germicidal Aerosols: II. Aerosol Centrifuge. S. R. Ginn and E. O. Powell.—p. 354.
Epidemiology of Hemolytic Streptococcus Infection in Relation to Acute Rheumatism: I. Hemolytic Streptococcus Epidemic and First Appearance of Rheumatism in a Training Center. C. A. Green.—p. 365.
Id.: II. Epidemic Rheumatism. C. A. Green.—p. 371.
Id.: III. Comparative Incidence of Various Infections and Acute Rheumatism in Certain Training Centers. C. A. Green.—p. 380.
Paratyphoid Fever: Epidemiologic Study. W. Savage.—p. 393.
*Immunization Against Typhoid and Paratyphoid with Alcohol Killed, Alcohol Preserved and Heat Killed, Phenol Preserved, Vaccine. H. Climie.—p. 411.
Lipoid Antigens of Corynebacterium Diphtheriae and Corynebacterium Hofmanni. L. Hoyle.—p. 416.
Comparative Digestibility of Wholemeal and White Breads and Effect of Degree of Fineness of Grinding on the Former. T. F. Macrae, J. C. D. Hutchinson, J. O. Irwin, J. S. D. Bacon, and E. I. McDougall.—p. 423.
Disinfectant Activity of Caustic Soda. Betty C. Hobbs and G. S. Wilson.—p. 436.

Immunization Against Typhoid and Paratyphoid.—Climie compared the Vi antibody of full functional efficiency produced by ordinary alcohol preserved vaccine in nurses and civilian defense workers. Of 106 persons inoculated, 44 were given ordinary T. A. B. C. vaccine and 62 alcohol T. A. B. C. vaccine. The vaccines were given subcutaneously into the arm, at the insertion of the deltoid. There was comparatively little difference from the two vaccines in regard to O agglutinin response. Vi agglutinins were found in 14.4 per cent of the alcohol-vaccine cases, but none appeared in the heat killed, phenolized vaccine cases. There was no significant difference in the frequency of local reactions, but there were definitely less general reactions in the alcohol-vaccine cases.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

49:341-452 (Aug.) 1942

Clinical Study of Menstruation, with Special Reference to Primary Dysmenorrhea. Helen M. Taylor.—p. 341.
Observations on Etiology and Prophylaxis of Prothrombin Deficiency and Hemorrhagic Disease in Newborn. A. I. S. Macpherson.—p. 368.
Importance of Increased Production and Excretion of Gonadotropic Hormone for Diagnosis of Hydatidiform Mole. B. Zondek.—p. 397.
*Dystocia Dystrophia Syndrome. B. Williams.—p. 412.
Splenic and Renal Aneurysms Complicating Pregnancy. R. A. Lennie and H. L. Sheehan.—p. 426.
Secondary Abdominal Pregnancy: Notes on Case. E. R. Wide.—p. 437.
Some Changes at the Rotunda Hospital Since 1926. B. Solomons.—p. 439.

Dystocia Dystrophia Syndrome.—Williams reports 62 cases of dystocia dystrophia encountered in eight years at five maternity hospitals. The incidence is difficult to judge, as only the more striking cases are likely to attract attention. The average age was 28. Details about the previous history were deficient, but a high incidence of menstrual irregularity and sterility was reported. Only 1 of the patients had had a previous full time pregnancy, and it ended in a cesarean section; 4 had had five miscarriages and 8 are known to have had a subsequent pregnancy, only 3 of whom had a normal delivery. The clinical condition was a contracted pelvis in 15, a funnel pelvis in 10 and a flat pelvis in 1. Toxemia occurred in 36, there was a trace of albumin in 7, increasing edema occurred during labor in 3, edema of the vulva was often prominent and eclampsia occurred in 7. Strong pains at the end of the first and during the second stage in these patients in whom disproportion and malposition are common are probably responsible for precipitating eclamptic fits by raising the blood pressure in an already preeclamptic patient. In 51 the time of the onset of labor was known and in 1 it commenced eight days prematurely, in 3 on the expected date and in 47 on an average of seventeen days after the expected date. The average length of the first and second stages of labor in the 46 in whom it was known was more than fifty hours. Forceps was applied in 48, lower segment cesarean section was performed in 8, a breech presentation occurred in 1, cleidotomy was done in 3 and a destructive operation was performed in 2. The method of delivery gives but little idea of the difficulty of carrying it out on these patients. Usually a high transversely arrested head, the so-called persistent occipitoposterior, was to be dealt with. Delivery without episiotomy or extensive laceration and trauma was impossible. The third stage of labor was infrequently complicated. The morbidity in 38 with complicated deliveries was usually due to infection of pelvic origin or of the wound from cesarean section. There were 2 instances of septicemia, 3 of paralytic ileus, 1 of volvulus of the pelvic colon, 1 of puerperal mania, 1 of mania, 1 of massive collapse of the lungs, 2 of phlebitis and 3 of mastitis. Forty-three of the 62 babies were male and 19 female: 21 were stillborn and 4 died. Examination of 17 of the stillbirths showed tentorial tears in 9, maceration in 5 and spina bifida in 1. Of the four neonatal deaths, one was due to a staphylococcic infection, in 1 a ventricular hemorrhage was found and of the 2 in whom postmortem examination was not carried out 1 is described as having had "convulsions." Of the babies that survived, many showed a large caput succedaneum and considerable molding. Asphyxia at birth and signs of cerebral irritation in the first few days were common. One had a fractured clavicle and 1 Erb's paralysis. There was only one maternal death. The enormous risks to a fetus of vaginal delivery in these pregnancies should incline one toward cesarean section. If the pregnancy is extremely prolonged, cesarean section should be carried out before labor starts. When cesarean section is judged unnecessary or unsuitable, early vaginal delivery has fewer risks for the fetus in suitable surroundings and in skilled hands. Once the fetus is dead, craniotomy should be carried out.

Medical Journal of Australia, Sydney

2:111-128 (Aug. 15) 1942

Flies, Fleas and Lice. J. Davidson.—p. 111.
Hemoglobin Values in Blood of Newborn Infants. J. D. Hicks.—p. 117.
Corrective Aspects of Stammering. T. G. Leary.—p. 119.

2:129-160 (Aug. 22) 1942

The Bancroft Memorial Lecture—Rickettsial Diseases in Australia. F. M. Burnet.—p. 129.
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Neurotic Casualties in the Field. H. R. Love.—p. 137.
Comparison of Agglutinin Content of Rabbit's Serum After Injection of Liquid and Dried Serum of Rabbits Immunized with Human Group A Cells. Rachel Jakobowicz, Marjorie Bick and Lucy Bryce.—p. 143.

2:161-192 (Aug. 29) 1942

Must There Be a Revolution in Medical Practice? A. E. Lee.—p. 161.
Appliances for Use with Thomas Leg Splint. W. A. Pryor.—p. 166.
Respirator "Clip-Ins." J. B. Hamilton.—p. 167.
Acute Infections of Upper Respiratory Tract in South Australia: II. Experiences During 1941. Jessica Mawson.—p. 168.
Symptomatology and Treatment of Bites of Australian Snakes. C. H. Kellaway.—p. 171.

Tubercle, London

23:155-170 (July) 1942

Treatment of Tuberculous Affections in Neck. H. Dodd.—p. 155.
Past Developments in Treatment of Pulmonary Tuberculosis. S. V. Pearson.—p. 159.

Der deutsche Militärarzt, Berlin

6:129-192 (March) 1941. **Partial Index**

Therapeutic Results in Fractures of Tibial Head. W. Müller.—p. 134.
Fatigue Injuries of Skeletal System in Soldiers. H. Stein.—p. 135.
Traumatic Origin of Spondylolisthesis. F. Scheid and Malluche.—p. 136.
*Mechanism of Dissemination of Gas Gangrene Bacilli in Human and Animal Organism. H. Lippelt.—p. 144.
Tonsillectomy in Peritonsillitis: Military Aspects. B. Kecht.—p. 155.
*Experiences in Two Outbreaks of Dysentery in Camps. Dötzer and Schuller.—p. 160.
*Group Determination from Dried Serum Drops in Mass Examinations, Especially of Recruits. G. F. Wagner.—p. 164.

Gas Gangrene Bacilli in Human and Animal Organism.—Lippelt points out that infections with diphtheria, tetanus and gas gangrene bacilli are unique in that the clinical picture is determined not so much by the organisms as by their toxins. The opinion still prevails that the causal organisms develop almost exclusively at the site of their first localization and that they send their toxin into the organism but without the tendency to invade the blood stream and the internal organs. Opinions regarding the pathogenesis of diphtheria have undergone a change. It has been suggested that the causal organism first enters the blood stream and is then eliminated secondarily by the tonsils. It has been found that diphtheria is not a sepsis, that it produces no metastases and that it is rather a bacteremia. The problems of tetanus bacilli are much more difficult. The first world war did not solve them. Twenty years later Mayer and Graetz were able to show that tetanus infection is a bacteremia. Mayer rejects the theory that agonal or postmortem invasion is responsible for the presence of tetanus bacilli in the heart blood and in the internal organs. He demonstrated the intra vitam invasion of the blood stream with tetanus bacilli. The problem of gas gangrene was investigated during the positional war at the Maginot line during 1939 and 1940. The investigators originally believed that gas gangrene bacilli develop locally in the wound and that toxins enter the body only from there. Systematic studies revealed that the organisms are found not only in the wound itself but removed far from it in apparently normal tissues, in the internal organs and in the blood stream. In 1 case they were detected on the amputation stump immediately after the operation, the amputation having been performed far away from the wound in the healthy part of the extremity. The general condition of this patient was satisfactory. In another case, in which amputation was performed because the wound had completely destroyed the circulation of the lower extremity, the bacteriologic and microscopic examination of the amputated extremity revealed the presence of a severe gas gangrene infection. There were no general symptoms to correspond to the severity of the infection, because of the interrupted circulation between the body and the infected leg. Observations on amputated extremities and necropsy material supported the assumption that the bacilli of the gas gangrene group are disseminated over the entire body by way of the blood stream. Rabbits were used to test the pathogenicity of the freshly cultured gas gangrene bacilli. At the same time observations could be made on the time that elapses between the infection and the appearance of the bacteremia and about the regularity of the positive bacteriologic test in the circulating blood and in the internal organs. The results indicate that gas gangrene is not a sepsis in Schottmüller's sense because there are no metastases. Observations in cases of gas gangrene with positive blood cultures convinced the author that even extensive surgical interventions had little effect. Likewise attempts at energetic serum therapy with the available serums seem to be ineffective. Omission of these measures, nevertheless, must be regarded as an error. In toxigenic infections (diphtheria, tetanus and gas gangrene) emphasis must be placed on early and energetic prophylaxis.

Dysentery in Camps.—Dötzer and Schuller report an epidemic of dysentery in a camp. Several mild cases had appeared from the middle of October until the end of December. On December 28 an epidemic suddenly flared up. Until the evening of this day 480 men, or 20 per cent of the inmates, had severe dysentery with temperature up to 105.8 F., chills and severe diarrhea. At the end of the week 30 per cent of the inmates were ill. The source of infection was probably a potato salad that had been prepared by a cook who was suffering from mild diarrhea. It was impossible to examine the potato salad bacteriologically, but the examination of the cook disclosed that he was a carrier of dysentery bacilli. The mortality of the dysentery was slight, amounting to 3 per thousand. The incubation period was three days in the fulminating cases and four to six days in others. The average duration was from two to three weeks. At the end of the second week many of the patients had edema of the ankles and of the face resembling hunger edema. Neuritic disturbances, chilliness, formication, drawing and piercing pains, and muscular weakness were frequent. Dehydration was mild or moderate. Patients with high fever frequently presented labial herpes. There were also conjunctivitis, stomatitis, gingivitis, burning of the bladder and urge to urinate, without pathologic findings in the urine, and swelling of the inguinal lymph nodes of the left side. After the acute symptoms had subsided there were frequently mild gastritis, dull pain in the epigastrium and subicterus. Bacteriologic studies disclosed dysentery bacilli of the Flexner group. The intestinal smear was twice as exact in demonstrating dysentery bacilli as the simple fecal smear. The bacteriologic demonstration of bacilli during the first three days is comparatively simple. Later it becomes difficult. Quarantine was instituted at once in order to prevent the spreading of the dysentery beyond the camp. Feces was disinfected with chlorinated lime and saponated solution of cresol. All sewage was subjected to chlorination. The kitchen personnel had been examined at the onset and 2 bacillus carriers were excluded. The food was sent from the kitchen in closed containers. Soiled dishes were disinfected with saponated solution of cresol. With the strict enforcement of hygienic measures the epidemic was brought under control in six weeks. At the time the quarantine was lifted 8 bacillus carriers still remained in isolation, but in the course of two weeks they had been rendered bacillus free. The most important therapeutic measures were bed rest and diet. On the first day a purge and fasting were usually prescribed. From the second day until the subsidence of the acute symptoms the patients were given first gruels and later puréed foods; the normal diet was gradually resumed. Circulatory remedies were of little effect. Intravenous injection of sodium chloride solution proved helpful, as did high enemas, rivanol, acriflavine hydrochloride and a 2.5 per cent soap solution. Rivanol proved effective in bacillus carriers. Resistance influenced by an adequate vitamin content of the food is of great importance in the favorable outcome.

Blood Group Determination from Dried Serum Drops.—Wagner points out that for mass examinations approved test serums are sometimes difficult to obtain. He decided to try dried test serum. After the necessary preliminary testing the serum is dropped on white card paper and spread to the size of a small coin. One drop each of test serums A, B and O are placed at distances of about 30 mm. from center to center. After the drops have been carefully dried they are ready for use. Although the length of preservability is not definitely known, it is probably at least two months. Simple drying at 37 C. of 0.05 cc. of undiluted serum yields a product that will produce noticeable reactions even in serums with moderate power of agglutination. The following procedure is employed in the determination of the blood group: 1. A large drop of isotonic solution of sodium chloride is placed with a pipet on each of the dried drops of serum and is left to stand for one minute. 2. Into each drop of the sodium chloride solution there is then placed a small drop of the blood to be tested. It is stirred at the same time at which the sodium chloride solution is spread over the dried serum drop. The blood is taken up with the three corners of a slide. A dilution of 1:5 is aimed at. 3. Good mixing is obtained by a mild movement of the card. 4. The result (agglutination) should be read not before five minutes have elapsed. This dried drop test is a handy form of blood group determination. The card method has the special advantage that the test results can be preserved on the card after drying of the blood serum mixture. The blood drops can be protected against damage by covering them with thin collodion. The card can be kept.

Book Notices

Roentgen Treatment of Infections. By James F. Kelly, M.D., F.A.C.R., Professor and Director of the Department of Radiology, Creighton University School of Medicine, Omaha. With the collaboration of D. Arnold Dowell, M.D., Assistant Professor of Radiology, Creighton University School of Medicine. Cloth. Price, $6. Pp. 432, with 122 illustrations. Chicago: Year Book Publishers, Inc., 1942.

While the employment of roentgen irradiation in the therapy of skin and neoplastic diseases has been adequately covered, no textbook is available on the roentgen treatment of the infections. Although roentgen therapy should occupy a prominent place in the treatment of certain types of infections, the definite beneficial and, at times, remarkable results are not generally appreciated. The importance of accurate technic in the treatment of these diseases is too frequently overlooked, and this method of therapy is judged by the results obtained following the careless administration of an unknown or improper dose. The appearance of this volume fills a definite place in the literature of roentgen therapy, and it is especially fitting and proper that it is presented by the authors, who have been pioneers and who have contributed so much to the subject. The names of Drs. Kelly and Dowell have been associated with the roentgen therapy of gas bacillus infection for a number of years, and a large portion of the book is devoted to this important subject.

This volume is divided into five parts. Part I, on x-ray physics and fundamentals, is concerned with the dosage factors, which are so important in the efficient administration of therapy in these conditions. The intrinsic and extrinsic factors affecting the tissue dose are carefully considered.

In part II the early and present uses of roentgen therapy are discussed. The chapter on the clinical features of roentgen therapy of infections is of considerable value. The description of mobile apparatus and the military use of the x-rays are timely subjects and should serve to limit casualties and deformities.

Part III is devoted to gas bacillus infection and is the outstanding portion of the book. The history, diagnosis, mortality and the surgical and roentgen therapy of gas bacillus infection are discussed. Comparisons are made of the results obtained in animal experiments and in human cases following surgery, serums, sulfanilamide and roentgen irradiation and in various combinations for prophylaxis and therapy. The authors conclude "that x-rays alone offer the ideal and most effective means of treatment. Serum is nonessential; amputation and débridement during the acute phase are detrimental. Sulfanilamide and its early derivatives are also highly detrimental." Uniformly consistent results have not always been obtained in clinical cases and animal experiments. Case reports discussed in sufficient detail are employed throughout to illustrate the authors' statements. The importance of individualizing each case treated by x-rays is emphasized.

Various types of abdominal infections, such as peritonitis, are discussed in part IV. As in previous sections, case reports with reproductions of roentgenograms and clinical records are included. Part V includes a miscellaneous group of infections, such as parotitis, mastoiditis and pneumonias.

Part VI considers the contraindications to the use of x-rays and contains a brief review of the literature. The authors conclude that the results following x-rays alone are always better than those obtained by the use of sulfanilamide and roentgen therapy. It was noted that the usual good results following x-rays were absent if sulfanilmide was being administered to the patient. The review of the literature and the list of contributors in the last section offer additional evidence of the authors' conclusions in the foregoing sections.

In general, the illustrations are good and the text is clear and concise. This volume should prove of inestimable value to the industrial and military surgeon and radiologist who see or expect to see cases of gas bacillus infection. Since every physician, regardless of specialty, is concerned with infections, this presentation of experimental, clinical and bibliographic evidence of the value and technic of an effective agent in a large group of crippling and fatal diseases should merit universal consideration. It is a necessity to any physican who attempts the roentgen treatment of infections.

The Clinical Application of the Rorschach Test. By Ruth Bochner, M.A., and Florence Halpern, M.A., Psychologist, Bellevue Psychiatric Hospital, New York. Introduction by Karl M. Bowman, M.D., Professor of Psychiatry, University of California Medical School, San Francisco. Cloth. Price, $3. Pp. 216. New York: Grune & Stratton, 1942.

The avowed purpose of this book, as stated in the preface, is to make the Rorschach test "available to all psychologists and psychiatrists." It is therefore warrantable to evaluate it in terms of the degree to which it accomplishes this rather ambitious aim. Perhaps, however, we should question the possibility or, indeed, the desirability of attempting to put this tool in the hands of any total group, whether composed of physicians or psychologists. This is not at all to concede, as surprisingly enough the authors seem to, that the Rorschach has been a cult which only the initiated could serve but merely to recognize it as a technic fully as complicated as the reading of x-ray plates by the roentgenologist and therefore properly the function of the specialist.

But, laying this question aside, how well does the book succeed in giving to any hitherto unenlightened person a working knowledge of the Rorschach test? Unfortunately it is not comprehensive enough or sufficiently precise for the beginning student and it is much too cluttered up with detail, too lacking in its presentation of underlying Rorschach philosophy, for the general reader. Not only for historical perspective but because it remains the single great classic in a rapidly growing literature, the student should begin with the Psychodiagnostik itself, now happily translated into English. This, followed with Oberholzer's article of twenty years ago in the *Journal of Nervous and Mental Disease*, will establish his firm foundation. Then if he keeps abreast of current material in the psychologic journals and the Rorschach exchange he will see both the many extensions in the use of the test and the new concepts which are being incorporated. Undoubtedly the best exposition of the subtleties and refinements of scoring which are used by members of the Rorschach Institute is embodied in another new book, The Rorschach Technique, by Klopfer and Kelley. The present book, then, like Beck's, which came out in 1937, is mainly useful in rounding out the picture with supplementary case material for those already familiar with Rorschach practice.

What is still lacking and what the psychologist called on to present and defend Rorschach personality studies and diagnostic impressions longs for is a new Rorschach classic, a small book like Hart's on insanity. Such a book, stripped of the details that obscure the forest, should present the philosophy of personality organization on which Rorschach theory is based and which constitutes its unique contribution. This is what should be "available" to all psychologists and psychiatrists but, unhappily, it is yet unwritten.

The Mentally Ill and Public Provision for Their Care in Illinois. By Stuart K. Jaffary, Director, School of Social Work, University of Toronto. The University of Chicago Social Service Monographs. Paper. Price, $1.25. Pp. 214. Chicago: University of Chicago Press, 1942.

In the first chapter of this monograph the author summarizes the organization existing in the state of Illinois for the care of the mentally ill prior to 1917. The second chapter discusses the department of public welfare. In the third and fourth chapters the state hospitals and their personnel are studied. The fifth chapter takes up admissions, paroles and discharges. The sixth chapter is an analysis of the development of social service in state hospitals. The seventh chapter takes in education, research and prevention. In the eight and ninth chapters, part 2, the facilities in the counties are discussed in relation to early examination, diagnosis, treatment and the commitment process. The tenth chapter considers the patient's return to his community. The eleventh chapter elaborates on the facilities in Cook County, Ill. There is an excellent detailed group of conclusions. The author feels, and justifiably so, that "the administration of the public services for the mentally ill in Illinois has been lacking in professional viewpoint and backward in leadership." The drafting of professional men from the medical schools in some instances and of professional men not connected with medical schools in other instances has proved to be full of gross shortcomings. These professional men lack leadership and because of this have permitted a continuation of a narrow policy of institutionalization in many of the hospitals. The author feels that the remedy lies in the

development of a sound professional point of view and direction, a workable department and leadership. With this the reviewer agrees. There is a good index and bibliography. This book is recommended to all the officials of the state of Illinois who are in any way connected with the direction and use of the state hospitals. There are myriads of tangible classified facts.

A Manual of Roentgen Diagnosis. By Kenneth S. Davis, M.S., M.D., Professor of Radiology, College of Medical Evangelists, Los Angeles. Second edition. Cloth. Price, $3.50. Pp. 160, with 279 illustrations. San Francisco: J. W. Stacey, Inc., 1941.

The expansion in teaching of roentgen diagnosis to undergraduates is producing a number of textbooks the use of which permits the limited hours to be available for demonstration purposes. Dr. Davis's book is a compilation of his own lecture notes, written in modified outline form, comprehensively and clearly presented. It is produced in lithotype and is small but generously illustrated. Obviously the scope is limited to the rudiments of roentgen diagnosis. Its intent is to give the undergraduate student a brief survey of the field, and in this effort success is achieved.

In an attempt to cover a subject within stringent limitations of space, the problem of selection of material looms large. The fact that approximately half of the book is devoted to diseases of the skeletal system reflects an unfortunate lag in the minds of many teachers who have not fully accepted the truly enormous expansion of roentgen diagnosis in the field of visceral lesions.

There are a few statements which are open to criticism. The distinction between a "fleck" and a "niche" in the diagnosis of duodenal ulcer may well be questioned. Likewise the categorical assertion that carcinoma "arising in an ulcer" is different from ulcerating carcinoma is unjustified. A more serious criticism is the failure to mention roentgenkymography and body section roentgenography or to detail bronchography. Not that the undergraduate need concern himself at length with these details of roentgen examination, but he should know what they are and their usefulness. Likewise, insufficient stress is given to the important question of the relative emphasis to be given roentgen examination in the weighing of the diagnostic problem.

The illustrations comprise drawings and reproductions of originals. They vary greatly in quality but, generally speaking, exhibit the lesions which they are intended to demonstrate. The author has wisely reproduced the roentgenograms in the negative, and the drawings have been photographed to maintain consistent densities throughout.

This is a satisfactory brief outline and should be useful as a teaching aid.

Preventive Medicine in Modern Practice. Edited under the Auspices of the Committee on Public Health Relations of the New York Academy of Medicine by James Alexander Miller, Chairman, George Baehr, Former Chairman, and E. H. L. Corwin, Executive Secretary. Being the Third edition, completely rewritten, of Outline of Preventive Medicine. Cloth. Price, $10. Pp. 851, with 22 illustrations. New York & London: Paul B. Hoeber, Inc., 1942.

The New York Academy of Medicine has taken an active interest in preventive medicine and public health for nearly a hundred years. As a result, its Committee on Public Health Relations has developed a quiet but powerful influence for good in New York City and, indirectly, throughout the United States. This committee has published a large, handsome volume. The book is the outgrowth of a previous publication under the auspices of the academy, "Outline of Preventive Medicine." The present edition consists of forty-nine chapters, with an excellent index. Each chapter is written by a different author. The editors first laid out the plan of the book and then requested each author to write on the special field in preventive medicine in which he is an authority. Most of the authors are members of the New York Academy of Medicine, but the editors have gone far afield and have chosen men from all parts of the nation to write special chapters.

The volume is divided into four parts: section I on sociobiologic aspects, comprising three chapters; section II, clinical aspects, thirty-two chapters; section III, environmental aspects, six chapters, and section IV, organizational aspects, eight chapters. The selection of titles for the chapters is excellent and the whole field of preventive medicine is considered. As always occurs in a book of this type, one encounters considerable variation in the quality of the material that is presented by the different authors. Some of the chapters have been written with the greatest precision and after a careful review of the subject: other chapters have been written more casually and without deep appreciation of the importance and value of available material. Furthermore, points of view and methods of presentation are sometimes at considerable variance. This is inevitable in a book of this type; as President Lowell once said, "Only one man can write a book." On the other hand, the multiple authorship gives the book a special value, since no one person could cover the enormous field of preventive medicine in an authoritative manner. The necessary unity and cohesion must be supplied by the editors—a difficult task, but one that has been well carried out.

The section on clinical aspects is the best. The whole purpose of the book is to focus the attention of medical men on the importance of incorporating preventive medicine in clinical practice. In this section, therefore, the authors have been most effective. It has been suggested that the other sections of the book might have been reserved for a second volume, which could be entitled "Public Health," for they deal more with community responsibility in health promotion than with the responsibility of the practicing physician in these matters.

The volume is well edited and beautifully printed. It does credit to its various authors and to the Academy of Medicine. The reviewer regrets that the book has one serious defect which may limit its usefulness as a textbook for medical students as well as a reference book for practicing physicians: its cost. Students, as a rule, are unable to purchase a ten dollar book, and practicing physicians do not yet appreciate the fact that it is well worth while to invest this sum in a book of this type. In this textbook the field is so well covered and the work so well done that, if studied carefully and referred to frequently, it will repay itself many times over.

Why We Have Automobile Accidents. By Harry R. DeSilva, Research Associate, Institute of Human Relations, Yale University, New Haven. Cloth. Price, $4. Pp. 394, with 55 illustrations. New York: John Wiley & Sons, Inc.; London: Chapman & Hall, Limited, 1942.

The American Medical Association has cooperated in every possible way with the authorities interested in cutting down the number of accidents occurring on the highways. Yet in this latest book on accident prevention, by a man who has done psychologic research in the field of traffic, almost no mention is made of the various committee reports and standards recommended by the American Medical Association. A wide variety of data are covered in this book from human engineering to mechanical engineering, from drivers' tests to the fiscal problems of highway building, which, while it has been covered adequately in a dispersed form in the periodical literature, has never been collected in a single volume. Such problems as speed on the highway, drivers' license testing, training of drivers and the factors involved in exposure to accidents are all systematically handled, but the human factors which interest the physician are not emphasized, probably because of the fact that the author is a psychologist and not a physician or psychiatrist. He has always been an advocate of mechanical testing of drivers, and the equipment which he built for this purpose has been exhibited at fairs and expositions. Yet in his book he frowns on that procedure and condemns it. While he stresses the driver, his emphasis lies on statistics rather than on the examination of persons, which is the *point d'appui* of the physician. No mention is made of the psychiatric examinations which have been made on thousands of drivers in psychiatric clinics connected with courts, although the clinics themselves are mentioned. The author does not recognize that psychobiologic mechanisms are important in traffic; i. e., that it is not speed which is important but the thinking processes which make the driver speed. Visual standards are only casually considered and then only from the points of view of visual acuity, tunnel vision and the effect of vitamins on vision. The book, which should have some value to traffic experts, has little for the physician who must decide on the basis of his examination whether the driver should or should not be permitted to continue to operate his motor car.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

EMERGENCY CARE OF FRACTURES AND SPLINTING

To the Editor:—I have found a good deal of confusion in circulation with regard to the use of the Thomas or similar traction splint, to be applied as a first aid measure in connection with civilian defense in the event of an enemy air raid or bombing. The Office of Civilian Defense medical bulletin number 2 makes no provision for this traction splint at the first aid post but only at the casualty station. It is well known that E. M. Cowell, who introduced the Thomas splint drill in the British army during the last war, reduced by this means a mortality from 70 to 40 per cent (in the field). The splint drill of the Royal Army Medical Corps training manual requires that the limb be splinted with traction before the patient is removed from the site of the injury. The slogan of the Committee on Fractures of the American Medical Association, "Splint 'em where they lie," is well known to those who visit the Scientific Exhibit at the annual sessions of the American Medical Association. My first question is Why should not these traction splints be in the list of the equipment recommended for the first aid posts, as recommended by the bulletin mentioned, as well as for the casualty station, as the latter is remote from the casualty and the first aid post is nearer the front line, where the critical work is done? If the answer should be that the splints should be only at the casualty station or by preference, please explain in full, for it is not always a surgeon who passes on the purchase of supplies for this purpose. My next question is Should a compound fracture with exposed bone be immediately treated in the field with a Thomas splint or similar traction splint? Several civilian surgeons have criticized this measure to me for the reason that in the compound fracture it would perhaps introduce sepsis if the end of the bone had penetrated the wound. Let us admit that the very nature of the casualty makes this a possibility and may require surgical débridement. The British instructions are not clear to me. Those I have read direct, in case of a wound, the cutting away of overlying clothing and dressing the wound, and, in case of severe hemorrhage, of control of hemorrhage before splinting. The American Red Cross first aid book, from which more than three million lay persons have had instruction (and hold certificates of proficiency—thus making them our critics), states that: "The splint [Thomas] should be used for all fractures from the hip to the ankle, . . . whether simple or compound" (p. 145). An even more explicit direction is given when the end of the bone protrudes (p. 137). We are informed that "In the last war about 30 per cent of all wounded men had compound fractures. This group is the largest of any major injury with which we have had to deal." We are informed of a definite change to a more serious character of the casualties of modern warfare, especially among undisciplined civilian populations. Hook discusses the subject of fractures with protruding bone among the fractures resulting from the raid at Pearl Harbor, where 48 per cent of the fractures were compound, 39 per cent comminuted and only 13 per cent simple. He leaves the question of the application of the traction splint to be decided by the availability of definitive treatment. This, of course, would be a matter of surgical judgment and discretion, the surgeon considering advantageous debridement not a part of Red Cross instruction. For the guidance of those physicians who are not actively engaged in traumatic surgery but who, living in target areas, must face tasks as well as the hazards of an open season for bombings, an answer or an opinion on the furnishing of this splint to civilian first aid posts and what hazards result from its use would be most helpful.

Richmond C. Holcomb, M.D., Upper Darby, Pa.

ANSWER.—This well worded, pertinent query should be widely read and thoroughly understood by all physicians, for who shall say where the target areas may be located?

Traction splints should be an important part of the supplies furnished first aid posts and first aid teams sent to trouble spots. There should, however, be some one on hand who has had instructions in the art of application of the splint and fixed tractions for transportation. An uninformed person might easily add to the difficulties of the injured individual by rough, unwise or incautious movement of the injured leg, failing to recognize that the principal purpose is first applying gentle and continued traction in the long axis of the leg, to be followed by support in the splint and substitution of the hand held traction of an assistant by the fixed tied-in traction from the loop about foot and ankle. Practically all the traction splints used by the Royal Army Medical Corps in the first phase of this war were applied by the enlisted personnel on the field; hence the slogan of the Committee on Fractures of the American Medical Association.

Traction splints should also be available at the casualty stations, because unsplinted individuals will arrive at these points; but a traction splint should be supplied at once, on arrival there, before any attempt is made to carry the patient farther, even into the hospital station or to x-ray examination.

A compound fracture should be treated at once on the field with a Thomas or similar traction splint, even if bone protrudes from the wound and its reintroduction into the soft tissues might carry in some infection. Such infection tends to remain local; it can often be controlled by the now universal use of the sulfonamide drugs spread onto the wound. Furthermore, such possible infection is probably not comparable in any way with the dangers of jarring, churning of bone in wounds, pain, increased hemorrhage and shock incidental to misguided efforts at transportation without a splint. All compound injuries are to be given débridement on reaching the casualty station or hospital where definitive treatment really starts. Hemorrhage at the site of injury may be controlled by firm pressure from sterile pack or dressing, rarely requiring use of a constrictor. On the fields of France many compound wounds thus splinted were transported for miles, and without the help of sulfonamide drugs. The results were as stated by the questioner. Débridement is not intended for Red Cross instruction—it is a surgical procedure.

SUBLINGUAL ADMINISTRATION OF MORPHINE

To the Editor:—I am interested in getting information on the relative value of morphine sulfate given by mouth and by hypodermic. This subject is of great importance to medical officers who are working in the field.

M. Abrams, Major, M. C., A. U. S.

ANSWER.—Morphine sulfate taken by mouth is completely and rapidly absorbed from the stomach and upper bowel. After absorption part of the morphine is excreted into the gastrointestinal tract. Morphine is quite rapidly destroyed in the body.

The sublingual adminstration of drugs offers a rapid route for the introduction of certain drugs into the systemic circulation. It is a much more direct route than through the stomach. The sublingual space is covered with a thin membrane of considerable extent. The network of large veins gives a free return of blood. In addition, the sublingual membrane is smooth, not furred like the tongue, nor is it covered with thick mucus or débris, as the stomach may be during a gastric upset.

When absorbed sublingually the drug escapes the action of the gastric ferments and, more important, it escapes the destructive action of the liver cells. In the case of morphine sulfate the liver through sulfonation causes a considerable loss in therapeutic activity.

If the mouth is too dry it may be rinsed with water. The hypodermic tablet or powdered drug is placed under the tongue just back of the teeth and the tongue is allowed to drop back into place. It is held in this position for a few minutes, although most of the drug will be absorbed in several seconds. The patient is advised not to swallow till the taste of the drug has disappeared. The effect will be felt quickly. The sublingual method of administering drugs has the advantage that it is quick, easy, safe, clean and reliable. It requires no special preparation, such as sterilization, and can be used by nonmedical persons.

Only those drugs which are effective in small doses, soluble and not irritating are suitable for sublingual administration. Morphine sulfate is ideal for this method.

RESISTANT THRUSH

To the Editor:—A patient with thrush (Oidium albicans) has been having trouble for many months, and it does not seem possible to clear the infection completely. Methylrosaniline 1 per cent has been applied faithfully. Are there any other substances which might be tried? A strong solution of silver nitrate was unsatisfactory. There is a liberal vitamin intake. I have wondered whether roentgen therapy is possible. The lesions are principally on the tongue, but there is also some involvement of the buccal mucous membranes.

M.D., West Virginia.

ANSWER.—The failure of thrush (Oidium albicans) to clear with the use of methylrosaniline is fairly common. Roentgen therapy is not generally known to be effective but would be worth a try, as it is in many infections when other methods have failed.

Several methods have been found occasionally successful. They include the use of compound solution of iodine applied at least once a day to the infected areas in the mouth, the use of potassium permanganate solution of various strengths and the use of sodium sulfathiazole ointment in 1 to 2 per cent strengths. The first of these three methods has definitely produced results and the last of the three methods is fairly recent but recommended and could be combined with the parenteral use of sulfonamides (preferably sulfadiazine).

The patient should be known to have an adequate dietary intake, and the gums and teeth should be kept scrupulously clean without trauma. The presence of syphilis, tuberculosis of the lungs or an underlying carcinoma should be excluded by appropriate measures. This would be especially required if the patient is an adult.

POSSIBLE MUCOCUTANEOUS RELAPSE OF LATENT SYPHILIS

To the Editor:—A man aged 48, who had been married twelve years, developed a chancre following intercourse with his wife. She admitted having been treated with mercurial inunctions and potassium iodide (only) over a period of several months in 1922. There were no symptoms or treatments afterward, and she considered herself cured. Would she be able to transmit the disease at so late a date? What are the chances of obtaining a negative blood test from her? M.D., Illinois.

ANSWER.—It is not actually impossible that this patient, married for twelve years to a woman who had contracted syphilis eight years previously, contracted syphilis from her twelve years after marriage. The only likely circumstance, however, under which this might occur is the presumption that the woman developed an infectious mucocutaneous relapse twenty or more years after her own infection; and, moreover, that she had not developed any such relapse until the twentieth year or later.

Ninety-five per cent or more of all infectious mucocutaneous relapses occur within the first four years of the infection. Late examples, indeed as late as the twenty-fifth year, have been reported, but they are extraordinarily rare and they tend to occur in patients who are chronic relapsers, that is, who have had multiple relapses over a period of years.

The chance of "obtaining a negative blood test from her" depends entirely on the status of her own syphilitic infection (that is to say, the presence or absence of neurologic, visceral or osseous involvement), and the kind of treatment given. Generalizations are not possible.

SHOCK IN CORONARY THROMBOSIS—EXERCISE AFTER CORONARY THROMBOSIS

To the Editor:—Having had a coronary thrombosis myself at a comparatively early age, I write to ask two questions: 1. It is now clearly recognized that transfusions of blood or plasma are of greatest importance in combating almost all forms of shock, whether associated with hemorrhage or not. Would not such transfusions be useful in the treatment of the shock associated with the early phase of coronary occlusion? Have they ever been tried? 2. According to the theory of Dr. Timothy Leary, the atherosclerosis which is a major factor in the production of coronary thrombosis is associated with fat metabolism. This would tend to agree with the common observation that coronary thrombosis is more common in those leading a sedentary life who do not burn up fat properly. Would it not be advisable, therefore, to increase rather than decrease the amount of exercise for those who have recovered from one attack of coronary thrombosis without anginal pain or any signs of decompensation in order to burn up the fat more completely? M.D., Colorado.

ANSWER.—1. It would not at first thought seem feasible to treat the shock associated with acute coronary occlusion with transfusions of blood or plasma, because in this particular group of cases it is the involvement of the heart itself that is responsible for the shock. Usually that involvement is extensive if shock is produced, and at least some of the actual circulatory failure at such times is of cardiac origin. Hence to load the circulation up with additional fluid may unduly increase the work of the heart and precipitate further heart failure. It might, however, be cautiously tried out in certain cases if it could be shown that the shock in such cases is wholly vascular. Reports of such treatment have not been found.

2. Exercise in moderation after complete healing of myocardial infarction which has left no aftermath of serious cardiac enlargement or limitation of coronary or myocardial reserve is probably desirable in the effort to maintain a good general state of health as well as to help to control obesity and to prevent a sluggish peripheral circulation.

CHRONIC SEMINAL VESICULITIS

To the Editor:—Is vasectomy of benefit in chronic unilateral nonspecific seminal vesiculitis? What role does a low grade stenosis of the duct have in nonspecific seminal vesiculitis? What therapeutic procedures or surgical procedures are indicated in stenosis of the duct? M.D., Georgia.

ANSWER.—As far as can be determined a vasectomy would not have any effect one way or the other on the progress of a nonspecific seminal vesiculitis. However, a stenosis of the ejaculatory duct emptying into the posterior urethra has much to do with the chronicity of seminal vesiculitis and obviously an infected area without adequate drainage will not respond to any sort of management and the treatment; hence the dilation of the ejaculatory ducts with bougies. This is now being routinely done for this purpose and is the most common procedure now used for the treatment of seminal vesiculitis with duct obstruction. The old Belfield operation of vasostomy and injection of antiseptic substances which would reach the vesicle has not been popular of late and its benefits are considered doubtful.

Seminal vesiculectomy has been considered under these conditions and still is valuable as a surgical procedure of considerable benefit in carefully selected cases.

CIRCULATION TIME AND CARDIAC OUTPUT

To the Editor:—On page 136 of the *Reader's Digest* for October 1942 it is stated that the blood travels the body circuit in seventeen seconds. Will you kindly tell me just how long it takes the blood to make the complete circuit and how much blood the heart pumps at each contraction? George W. Reese, M.D., Sunbury, Pa.

ANSWER.—The inquirer doubtless realizes that there is not any accurate way to determine total circulation time. Figures recorded vary with the technic used. One author gives twelve to twenty-eight seconds, average twenty-five seconds. Other authors give much lower figures, such as fifteen to seventeen seconds. The total time is of less practical significance than the time for limited parts of the circuit, such as arm to lung or arm to carotid sinus.

The heart ejects 3 to 4 liters per minute. At the average figure of 3,500 cc., at 70 beats per minute the stroke volume would be 50 cc. There are important qualifications on all of the statements. The inquirer should consult any good textbook on physiology for a fuller discussion than can be given here.

RADIOACTIVE STRONTIUM

To the Editor:—Will you please give me any information you may have concerning the use of radioactive phosphorus or radioactive strontium in cases of multiple myeloma? Is it possible to obtain any at the laboratories? W. T. Thornton, M.D., Missoula, Mont.

ANSWER.—Radioactive strontium provides a means of giving selective beta irradiation to lesions of bone and bone marrow, since the element, like calcium, localizes in bone. Its use is in the experimental stage, and, if and when it proves to be of great therapeutic value, it will become generally available. At present it is most readily made in a cyclotron, and there are several of these machines distributed throughout the United States, including those at the University of California, University of Michigan, Ohio State University and Howard University. As far as is known, no commercial laboratory handles the material.

OILS OF RETENTION ENEMAS

To the Editor:—With the price of "pure imported olive oil" sky high, is there any reason why pure domestic cottonseed or peanut oil should not be used for enemas in children? If so, what can be substituted for olive oil? J. J. Horton, M.D., Buda, Texas.

ANSWER.—There is no reason why the oils mentioned should not be used. Perhaps safer, because nonallergic, would be the ordinary hydrocarbon oil. Doubtless retention enemas are being thought of. For ordinary cleansing enemas, isotonic solution of sodium chloride is best.

REMOVAL OF NEEDLE FRAGMENT FROM DELTOID

To the Editor:—I noticed on page 326 of the September 26 issue of The Journal note about a fragment of needle in the deltoid, asking the best procedure for removal of the fragment if it is necessary to remove it. I agree that it is wise to leave the needle alone if it does not cause trouble, but if it becomes necessary to remove it the operation is by no means simple. I shoula like to offer some suggestions. When a foreign body is sufficiently large to be recognized under the fluoroscope, its removal with fluoroscopic aid should be a simple matter. A puncture incision, perhaps a half inch in length, should be made at the site elected for the best approach. Then under fluoroscopic control a suitable forceps, preferably one with long jaws, fairly narrow at the point, should be insinuated into the tissues through this opening in the skin in the direction of the needle, fluoroscopic glimpses being made from time to time to show that the forceps is being pushed in the right direction. When the end of the retrieving forceps has approached the vicinity of the needle, the x-ray tube should be rocked back and forth underneath the table while the movements of the needle and of the end of the forceps are observed on the screen (parallax method). It is important that the shutter be opened to provide a very small slit opening, thus limiting to the minimum the illuminated area on the screen and thus protecting the hands of the surgeon. Naturally a sterile sheet or towel will be interposed between the screen and the surgical field. In the parallax method the object nearer the screen will undergo less movement than the object farther from the screen; thus it will be easy to know when the end of the forceps and the end of the needle are in the same plane; by rotating the patient to secure still further guidance, one may grasp the end of the needle in the forceps and lock it, after which the forceps and the needle together can be withdrawn. If the surgeon is not accustomed to this method, a little practice beforehand with a small needle fragment buried in an ordinary piece of meat will give him the necessary experience. This method has the advantage of necessitating only a puncture wound in the skin. A local anesthetic is sufficient. However, it has been my experience that a small piece of a hypodermic needle broken off in the gluteal muscles is not easily visible on the fluoroscope, especially in heavy persons. Under such circumstances the fluoroscopic method is probably inadvisable. A simple procedure consists in the introduction of two or three long straight needles into the part, aiming at the region where the fragment of the needle is known to lie. Stereoscopic films may then be made and the relation of the foreign body to the guide needles determined. Then, under appropriate anesthesia, leaving these guide needles in place, the offending hypodermic needle may be found without complication. I have usually found a local anesthetic adequate. James T. Case, M.D., Chicago.